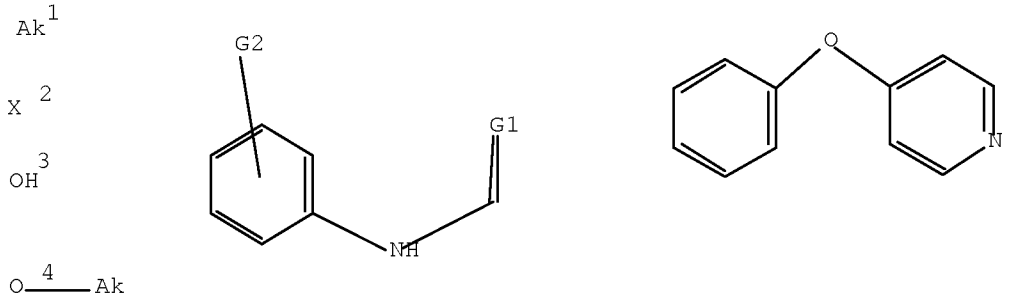
***** INVENTOR RESULTS *****

=> d his l78

(FILE 'HCAPLUS' ENTERED AT 13:24:34 ON 16 JUL 2008)
L78 5 S L77 NOT L54

=> d que l78
L1 1 SEA FILE=HCAPLUS ABB=ON PLU=ON US20070142440/PN
L47 STR



G1 O,S
G2 [@1],[@2],[@3],[@4],[@5]

Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str

chain nodes :
7 8 9 22 24 25 26 27 28 29 36
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21
chain bonds :
6-7 7-8 8-9 14-22 18-22 27-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21
17-18 18-19 19-20 20-21
exact/norm bonds :
6-7 7-8 8-9 14-22 18-22 27-28

```
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  10-11  10-15  11-12  12-13  13-14  14-15  16-17  16-
21
17-18  18-19  19-20  20-21
isolated ring systems :
containing 1 : 10 : 16 :


G1:O,S

G2:[*1],[*2],[*3],[*4],[*5]

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:CLASS  8:CLASS  9:CLASS  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:Atom
20:Atom  21:Atom
22:CLASS  24:CLASS  25:CLASS  26:CLASS  27:CLASS  28:CLASS  29:CLASS  36:CLASS
37:Atom




L48             SCR 2043 AND 1918 AND 2050
L50          1662 SEA FILE=REGISTRY SSS FUL L47 NOT L48
L52           607 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L50
L53           584 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L52 AND PHARMAC?/SC,SX
L54            64 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L53 AND (AY<2004 OR PY<2004
                  OR PRY<2004)
L69            22 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BURGDORF L?/AU
L70            45 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BUCHSTALLER H?/AU
L71            36 SEA FILE=HCAPLUS ABB=ON  PLU=ON  STIEBER F?/AU
L72            28 SEA FILE=HCAPLUS ABB=ON  PLU=ON  AMENDT C?/AU
L73           202 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GREINER H?/AU
L74           150 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GRELL M?/AU
L75            38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SIRRENBERG C?/AU
L76             3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ZENKE K?/AU
L77            10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (((L69 OR L70 OR L71 OR L72
                  OR L73 OR L74 OR L75 OR L76)) AND L52) OR (L1 AND L52)
L78             5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L77 NOT L54


=> d his l107

     (FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 13:48:43 ON 16 JUL 2008)
L107            3 S (L100-L106) AND  TYROSINE KINASE?

=> d que l107
L100            9 SEA BUCHSTALLER HANS PETER/AU
L101            8 SEA STIEBER FRANK/AU
L102            7 SEA AMENDT CHRISTIANE/AU
L103           14 SEA GREINER HARTMUT/AU
L104           70 SEA GRELL MATTHIAS/AU
L105           19 SEA SIRRENBERG CHRISTIAN/AU
L106            2 SEA ZENKE FRANK/AU
L107            3 SEA ((L100 OR L101 OR L102 OR L103 OR L104 OR L105 OR L106))
                  AND TYROSINE KINASE?


=> dup rem l78 l107
FILE 'HCAPLUS' ENTERED AT 13:53:35 ON 16 JUL 2008
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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE 'MEDLINE' ENTERED AT 13:53:35 ON 16 JUL 2008

FILE 'EMBASE' ENTERED AT 13:53:35 ON 16 JUL 2008
Copyright (c) 2008 Elsevier B.V. All rights reserved.
PROCESSING COMPLETED FOR L78
PROCESSING COMPLETED FOR L107
L109 8 DUP REM L78 L107 (0 DUPLICATES REMOVED)
ANSWERS '1-5' FROM FILE HCAPLUS
ANSWERS '6-7' FROM FILE MEDLINE
ANSWER '8' FROM FILE EMBASE

=> d l109 1-5 ibib abs; d l109 6-8 ibib ab

L109 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:817202 HCAPLUS Full-text
DOCUMENT NUMBER: 147:158473
TITLE: Use of integrin ligands and co-therapeutic agents for isolated organ perfusion combination therapy of cancer
INVENTOR(S): Goodman, Simon; Grell, Matthias; Ten Hagen, Timo L. M.; Egermont, Alexander M. M.
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 54pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007082742	A1	20070726	WO 2007-EP408	20070118

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2006-1049 A 20060118

AB The invention discloses a combination therapy for the treatment of tumors and tumor metastases comprising administration of integrin ligands, preferably integrin antagonists, together with co-therapeutic agents or therapy forms that have synergistic efficacy when administered together with the ligands, such as chemotherapeutic agents and/or radiation therapy, in isolated organ perfusion. The therapy results in a synergistic potential increase of the inhibition effect of each individual therapeutic on tumor cell proliferation, yielding more effective treatment than found by administering an individual component alone.

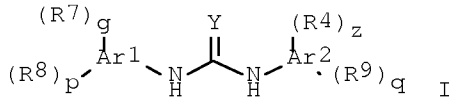
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L109 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:364321 HCAPLUS Full-text
DOCUMENT NUMBER: 144:412515
TITLE: Heterocyclic substituted bisarylurea derivatives as kinase inhibitors and their preparation, pharmaceutical compositions, and use for treatment of diseases mediated or propagated by kinases
INVENTOR(S): Stieber, Frank; Jonczyk, Alfred; Hoelzemann, Guenter; Buchstaller, Hans-Peter; Burgdorf, Lars Thore; Rautenberg, Wilfried; Greiner, Hartmut
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 232 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006040056	A1	20060420	WO 2005-EP10744	20051006
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005293839	A1	20060420	AU 2005-293839	20051006
CA 2584185	A1	20060420	CA 2005-2584185	20051006
EP 1799669	A1	20070627	EP 2005-789864	20051006
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 101039932	A	20070919	CN 2005-80035117	20051006
JP 2008515943	T	20080515	JP 2007-536047	20051006
MX 200704248	A	20070612	MX 2007-4248	20070410
KR 2007062998	A	20070618	KR 2007-708364	20070412
IN 2007KN01680	A	20070727	IN 2007-KN1680	20070511

PRIORITY APPLN. INFO.:	EP 2004-24369	A	20041013
	EP 2005-16845	A	20050803
	WO 2005-EP10744	W	20051006

OTHER SOURCE(S): MARPAT 144:412515
GI



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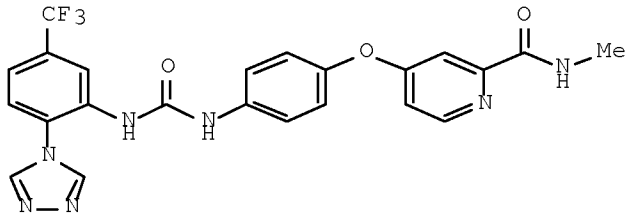


II

AB The invention relates to heterocyclic substituted bisarylurea derivs. of formula I, the use of the compds. of formula I as inhibitors of one or more kinases, the use of the compds. of formula I for the manufacture of a pharmaceutical composition and a method of treatment, comprising administering said pharmaceutical composition to a patient. Compds. of formula I wherein R4 is (X-Ar3)α-(R10)10; Ar1, Ar2, and Ar3 are independently 5- to 14-membered unsatd. or aromatic cyclic hydrocarbon, or 2- to 10-membered unsatd. or aromatic heterocyclic residue, preferably 1 to 5 heteroatoms selected from N, O, and S; α is 0, 1, or 2; r, z, and p are independently 0, 1, 2, 3, 4 or 5; R7 is nitrogen containing heterocyclic moiety bound directly to Ar1 via a nitrogen atom, etc.; R8, R9, and R10 are independently H, (alkoxy)alkyl, alkenyl, C3-7 cycloalkyl, alkenylcycloalkyl, halo, CH2halo, CH(halo)2, C(halo)3, NO2, etc.; Y is O, S, NH and derivs., (un)substituted CHNO2, (un)substituted CHCN, or C(CN)2; g is 1, 2, or 3; q is 0, 1, 2, 3 or 4; and their pharmaceutically acceptable derivs., salts and solvates thereof are claimed in this invention. Example compound II was prepared by chlorination and esterification of pyridine-2-carboxylic acid to give Me 4-chloropyridine-2-carboxylate, which underwent amidation with methylamine to give 4-chloropyridine-2-carboxylic acid methylamide, which was reacted with 4-aminophenol; the resulting 4-(4-aminophenoxy)pyridine-2-carboxylic acid methylamine reacted with p-nitrophenyl chloroformate and 4-(2-amino-4-trifluoromethylphenyl)-1,2,4-triazole to give example compound II. All the invention compds. were evaluated for their activity as modulators and inhibitors of kinases. From the assay, it was determined that these compds. preferably inhibit VEGF-stimulated mitogenesis of human vascular endothelial cells in cultures with IC50 values of 0.01-5.0 μM.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

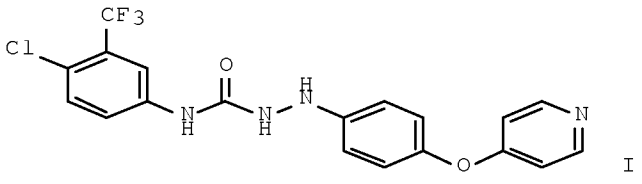
L109 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:977019 HCAPLUS Full-text
DOCUMENT NUMBER: 143:286162
TITLE: Preparation of aryl semicarbazide derivatives as kinase inhibitors
INVENTOR(S): Buchstaller, Hans-Peter; Finsinger, Dirk; Stieber, Frank; Wiesner, Matthias; Amendt, Christiane; Sirrenberg, Christian; Zenke, Frank; Grell, Matthias
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 278 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005082853	A1	20050909	WO 2005-EP1443	20050214
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005217041	A1	20050909	AU 2005-217041	20050214
CA 2557359	A1	20050909	CA 2005-2557359	20050214
EP 1727800	A1	20061206	EP 2005-715319	20050214
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007523928	T	20070823	JP 2007-500096	20050214

PRIORITY APPLN. INFO.: EP 2004-4330 A 20040226
WO 2005-EP1443 W 20050214

OTHER SOURCE(S): CASREACT 143:286162; MARPAT 143:286162
GI



I

AB Title compds. of formula A-D-B [D = bivalent semicarbazide moiety, or a derivative thereof; A = (un)substituted moiety L-(M-L1)n where L = 5-7 membered cyclic structure, preferably selected from the group consisting of aryl, heteroaryl, arylene, and heteroarylene, bound directly to D, L1 = (un)substituted cyclic moiety preferably selected from aryl, heteroaryl, aralkyl, cycloalkyl, and heterocyclyl, M = bond or bridging group, n = 0-4; B = (un)substituted, up to tricyclic aryl or heteroaryl moiety], and their pharmaceutically acceptable salts are prepared and disclosed as inhibitors of one or more kinases (no data). Thus, e.g., I was prepared by reaction of 4-chloro-3-trifluoromethylphenyl isocyanate with 4-(pyridin-4-yloxy)phenylhydrazine (preparation given). Further disclosures include the use of the compds. of the invention for the manufacture of a pharmaceutical composition and a method of treatment, comprising administering said pharmaceutical composition to a patient.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L109 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:823661 HCAPLUS Full-text
DOCUMENT NUMBER: 143:229726
TITLE: Preparation of 1,3-diarylureas as inhibitors of raf and other kinases useful against cancer and other diseases
INVENTOR(S): Buchstaller, Hans-Peter; Burgdorf, Lars; Stieber, Frank; Amendt, Christiane; Grell, Matthias; Sirrenberg, Christian; Zenke, Frank
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 264 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005075425	A2	20050818	WO 2005-EP387	20050117
WO 2005075425	A3	20061214		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005211448	A1	20050818	AU 2005-211448	20050117
CA 2554878	A1	20050818	CA 2005-2554878	20050117
EP 1730111	A2	20061213	EP 2005-700967	20050117
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1972925	A	20070530	CN 2005-80002901	20050117
BR 2005007198	A	20070626	BR 2005-7198	20050117
JP 2007519653	T	20070719	JP 2006-549997	20050117
US 20070161677	A1	20070712	US 2006-587292	20060725
MX 2006PA08449	A	20061002	MX 2006-PA8449	20060726
IN 2006KN02441	A	20070525	IN 2006-KN2441	20060828

PRIORITY APPLN. INFO.: EP 2004-2092 A 20040130
WO 2005-EP387 W 20050117
OTHER SOURCE(S): MARPAT 143:229726
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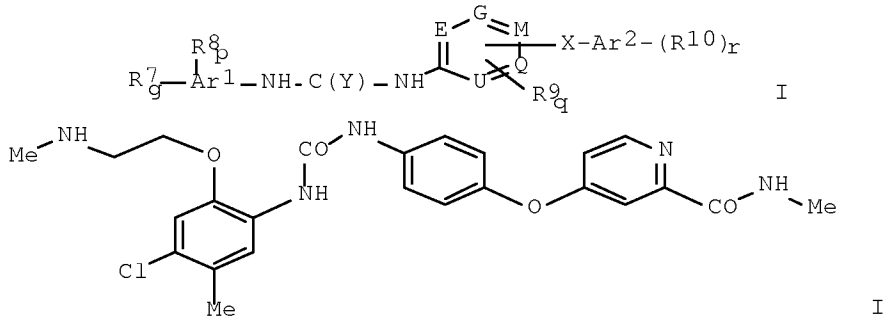

I

I

AB The present invention relates to bisarylurea derivs. (shown as I; variables defined below; e.g. 4-[4-[3-[4-chloro-5-methyl-2-(2-methylaminoethoxy)phenyl]ureido]phenoxy]pyridine-2-carboxylic acid methylamide (shown as II)), their use as inhibitors of raf-kinase (no data) and for the manufacture of a pharmaceutical composition and a method of treatment, comprising administering said pharmaceutical composition to a patient. Methods of preparation are claimed and >100 example prepns. are included. For example, 1-[2-[2-[(tert-butoxycarbonyl)(methyl)amino]ethoxy]-5-(trifluoromethyl)phenyl]-3-[4-[[2-(methylcarbamoyl)pyridin-4-yl]oxy]phenyl]urea was prepared (87 %) by reacting tert-Bu [2-[2-amino-4-(trifluoromethyl)phenoxy]ethyl](methyl)carbamate (preparation given) with p-nitrophenyl chloroformate followed by N-methyl-4-(4- aminophenoxy)pyridine-2-carboxamide (preparation given) and DIPEA; deprotection gave 86 % 1-[2-[2-(methylamino)ethoxy]-5-(trifluoromethyl)phenyl]-3-[4-[[2-(methylcarbamoyl)pyridin-4-yl]oxy]phenyl]urea. For I: Ar1, Ar2 = aromatic hydrocarbons containing 6 to 14 C atoms and ethylenic unsatd. or aromatic heterocyclic residues containing 3 to 10 C atoms and one or two heteroatoms, = N, O and S; E, G, M, Q and U = C and N atoms, with the proviso that ≥1 of E, G, M, Q and U are C atoms and that X is bonded to a C atom. R7 = Het, OHet, N(R11)Het, (CR5R6)kHet, et al. or R7 = -SO2-CR8:CR8-, wherein both valencies are bound vicinally to Ar1; R8, R9 and R10 = H, A, cycloalkyl comprising 3 to 7 C atoms, Hal, et al.; Y = O, S, NR21, C(R22)-NO2, C(R22)-CN and C(CN)2; g = 1-3, preferably 1 or 2, p, r = 0-5; q = 0-4, preferably 0, 1 or 2; addnl. details are given in the claims.

L109 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:982303 HCAPLUS Full-text
DOCUMENT NUMBER: 143:286291
TITLE: Preparation of 2-pyridinecarboxamides as kinase inhibitors
INVENTOR(S): Burgorf, Lars; Buchstaller, Hans-Peter; Stieber, Frank; Amendt, Christiane; Greiner, Hartmut; Grell, Matthias; Sirrenberg, Christian; Zenke, Frank
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: Ger. Offen., 33 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102004009238	A1	20050908	DE 2004-102004009238	20040226
AU 2005219496	A1	20050915	AU 2005-219496	20050113
CA 2557302	A1	20050915	CA 2005-2557302	20050113
WO 2005085202	A1	20050915	WO 2005-EP273	20050113
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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EP 1718614	A1	20061108	EP 2005-700886	20050113
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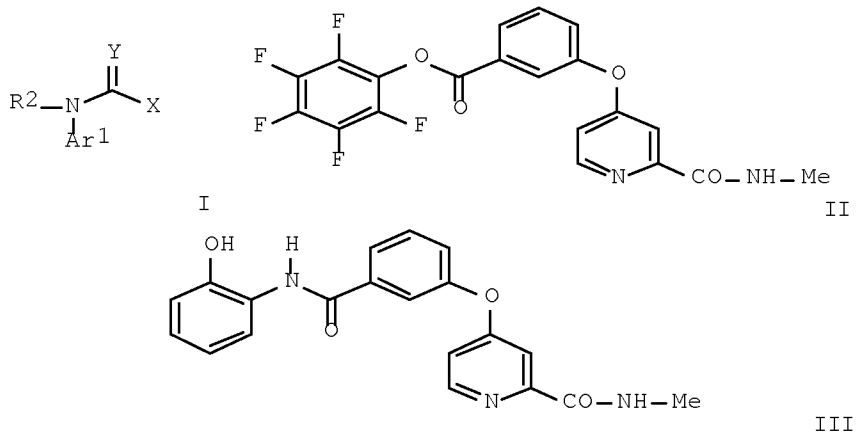
JP 2007523921	T	20070823	JP 2007-500077	20050113
US 20070142440	A1	20070621	US 2006-590724	20060825 <--

PRIORITY APPLN. INFO.: DE 2004-102004009238A 20040226
WO 2005-EP273 W 20050113

OTHER SOURCE(S): MARPAT 143:286291

GI



I II III

AB Title compds. I [X = Ar2-Z-Ar3; Ar1, Ar2, Ar3 = (un)substituted aromatic, het; R1 = H, aryl, O-aryl, etc.; R2 = H, A, alkylene-aryl, etc.; A = alkyl with provisos; Z = G1n, G1nEG2m, EG1nG2m, etc.; E = O, CO, C=N, etc.; G1, G2 = CR1R1, E; n = 0-5; m = 0-2] and their pharmaceutically acceptable salts and formulations were prepared For example, N-alkylation of 2-aminophenol with pentafluorophenol II afforded pyridinecarboxamide III in 13% yield. Compds. I are claimed to be effective inhibitors of the tyrosine kinases, in particular TIE-2 and VEGFR, and the Raf kinases.

L109 ANSWER 6 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2003332773 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12866072
TITLE: Multistep solid-phase synthesis of an antibiotic and receptor tyrosine kinase inhibitors using the traceless phenylhydrazide linker.
AUTHOR: Stieber Frank; Grether Uwe; Mazitschek Ralph; Soric Natascha; Giannis Athanassios; Waldmann Herbert
CORPORATE SOURCE: Max-Planck-Institut fur Molekulare Physiologie, Abteilung Chemische Biologie, Otto-Hahn-Strasse 11, 44227 Dortmund, Germany.
SOURCE: Chemistry (Weinheim an der Bergstrasse, Germany), (2003 Jul 21) Vol. 9, No. 14, pp. 3282-91.
Journal code: 9513783. ISSN: 0947-6539.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 17 Jul 2003
Last Updated on STN: 11 Sep 2003
Entered Medline: 10 Sep 2003

AB The hydrazide group is an oxidatively cleavable traceless linker for solid-phase chemistry. This linker technology was used to develop a multistep solid-phase synthesis of an antibiotic that is active against Mycobacterium tuberculosis. Furthermore, we describe an efficient method for the traceless synthesis of 2-aminothiazoles that display dual inhibitory activity against the receptor tyrosine kinases VEGFR-2 and Tie-2. The synthesis method proceeds through 9 steps on the solid phase and should give access to a much larger library of 2-aminothiazoles, from which a new class of anti-angiogenesis drugs may be developed.

L109 ANSWER 7 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2003043368 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12481350
TITLE: Traceless solid-phase synthesis of 2-aminothiazoles: receptor tyrosine kinase inhibitors with dual selectivity for Tie-2 and VEGFR-2.
AUTHOR: Stieber Frank; Mazitschek Ralph; Soric Natascha; Giannis Athanassios; Waldmann Herbert
CORPORATE SOURCE: Max-Planck-Institut fur molekulare Physiologie, Abteilung Chemische Biologie, Otto-Hahn-Strasse 11, 44227 Dortmund, Germany.
SOURCE: Angewandte Chemie (International ed. in English), (2002 Dec 16) Vol. 41, No. 24, pp. 4757-61.
Journal code: 0370543. ISSN: 1433-7851.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303

ENTRY DATE: Entered STN: 30 Jan 2003
Last Updated on STN: 19 Mar 2003
Entered Medline: 18 Mar 2003

L109 ANSWER 8 OF 8 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1996270766 EMBASE Full-text
TITLE: Neurotrophins stimulate the release of dopamine from rat mesencephalic neurons via Trk and p75(Lntr) receptors.
AUTHOR: Blochl, Andrea (correspondence); Sirrenberg, Christian
CORPORATE SOURCE: Max-Planck-Institute for Psychiatry, Department of Neurochemistry, D-82152 Martinsried, Germany. Bloechl@alf.biochem.mpg.de
AUTHOR: Blochl, Andrea (correspondence)
CORPORATE SOURCE: Max-Planck-Institute for Psychiatry, Dept. of Neurochemistry, Am Klopferspitz 18a, D-82152 Martinsried, Germany. Bloechl@alf.biochem.mpg.de
AUTHOR: Sirrenberg, Christian
CORPORATE SOURCE: Ludwig-Maximilian-University Munich, Dept. of Biochemistry, 80336 Munich, Germany.
AUTHOR: Blochl, Andrea (correspondence)
CORPORATE SOURCE: Dept. of Neurochemistry, Max-Planck-Institute for Psychiatry, Am Klopferspitz 18a, D-82152 Martinsried, Germany.
SOURCE: Journal of Biological Chemistry, (1996) Vol. 271, No. 35, pp. 21100-21107.
Refs: 64
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 Oct 1996
Last Updated on STN: 7 Oct 1996

AB We analyzed the short term effect of neurotrophins on mesencephalic neuronal cultures of embryonic (E14) rats with respect to which receptors mediate the actions. Brain-derived neurotrophic factor (BDNF) or neurotrophin-3 enhanced within minutes in a dose-dependent manner (2, 20, 100 ng/ml for 5 min) depolarization-induced (KCl, 30 mM 5 min) and basal dopamine release, but nerve growth factor (NGF) was only effective at high doses (100 ng/ml). The effect of BDNF, but not of NGF, was blocked by K252a or K252b. BDNF, but not NGF, phosphorylated trkB receptors. The NGF-induced, but not the BDNF-induced effect upon the release of dopamine was blocked by anti-p75 antibody MC192. C(2)-ceramide, an analogue of ceramide, the second messenger of the sphingomyelin pathway, and sphingomyelinase itself induced a release of dopamine comparable with the effect of NGF. NGF, but not BDNF, increased ceramide production. In addition, simultaneous treatment with BDNF and NGF led to a partial prevention of the NGF stimulated, p75(Lntr)-mediated effect. We conclude that BDNF stimulates the release of dopamine by activation of the trkB receptor, whereas NGF affects the release via the p75(Lntr) receptor inducing the sphingomyelin pathway.

***** QUERY RESULTS *****

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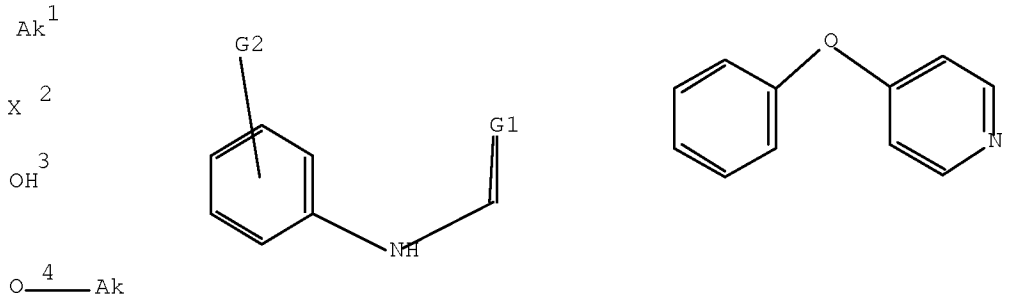
=> d que l54
L47 STR



G1 O,S
G2 [@1],[@2],[@3],[@4],[@5]

Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str

chain nodes :
7 8 9 22 24 25 26 27 28 29 36
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21
chain bonds :
6-7 7-8 8-9 14-22 18-22 27-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21
17-18 18-19 19-20 20-21
exact/norm bonds :

6-7 7-8 8-9 14-22 18-22 27-28
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21
17-18 18-19 19-20 20-21
isolated ring systems :
containing 1 : 10 : 16 :

G1:O,S

G2:[*1],[*2],[*3],[*4],[*5]

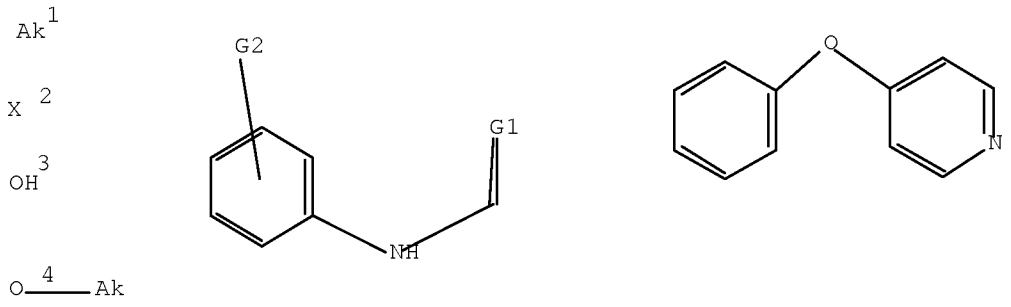
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom
22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 36:CLASS
37:Atom

L48 SCR 2043 AND 1918 AND 2050
L50 1662 SEA FILE=REGISTRY SSS FUL L47 NOT L48
L52 607 SEA FILE=HCAPLUS ABB=ON PLU=ON L50
L53 584 SEA FILE=HCAPLUS ABB=ON PLU=ON L52 AND PHARMAC?/SC,SX
L54 64 SEA FILE=HCAPLUS ABB=ON PLU=ON L53 AND (AY<2004 OR PY<2004 OR PRY<2004)

=> d his l86

(FILE 'BIOSIS' ENTERED AT 13:39:15 ON 16 JUL 2008)
L86 8 S L83 OR L85

=> d que l86
L47 STR



G1 O,S
G2 [@1],[@2],[@3],[@4],[@5]

Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str

chain nodes :
7 8 9 22 24 25 26 27 28 29 36
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21
chain bonds :
6-7 7-8 8-9 14-22 18-22 27-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21
17-18 18-19 19-20 20-21
exact/norm bonds :
6-7 7-8 8-9 14-22 18-22 27-28
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21
17-18 18-19 19-20 20-21
isolated ring systems :
containing 1 : 10 : 16 :

G1:O,S

G2:[*1],[*2],[*3],[*4],[*5]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom
22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 36:CLASS
37:Atom

L48		SCR 2043 AND 1918 AND 2050
L50	1662	SEA FILE=REGISTRY SSS FUL L47 NOT L48
L64	1797	SEA FILE=HCAPLUS ABB=ON PLU=ON (TIE2 OR TIE(W)2 OR VEGFR OR RAF) (W) (KINASE? OR KINASE INHIB?)
L79	1	SEA FILE=REGISTRY ABB=ON PLU=ON L50 AND (MEDLINE/LC OR BIOSIS/LC OR DRUGU/LC OR EMBASE/LC)
L81	89	SEA FILE=BIOSIS ABB=ON PLU=ON L79
L82	34	SEA FILE=BIOSIS ABB=ON PLU=ON L81 AND L64

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L83           3 SEA FILE=BIOSIS ABB=ON  PLU=ON  L82 AND (PREP? OR SYNTHES?)
L85           6 SEA FILE=BIOSIS ABB=ON  PLU=ON  L82 AND TYROSINE KINASE?
L86           8 SEA FILE=BIOSIS ABB=ON  PLU=ON  L83 OR L85


=> d his l98

     (FILE 'EMBASE' ENTERED AT 13:42:27 ON 16 JUL 2008)
L98          12 S L89 AND (AY<2004 OR PY<2004 OR PRY<2004)

=> d que l98
L47             STR
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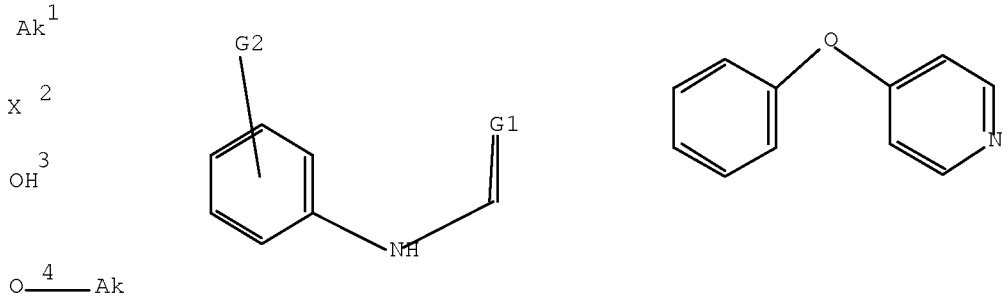


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G1 O,S
G2 [@1],[@2],[@3],[@4],[@5]
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Structure attributes must be viewed using STN Express query preparation:

Uploading L11.str

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chain nodes :
7  8  9  22  24  25  26  27  28  29  36
ring nodes :
1  2  3  4  5  6  10  11  12  13  14  15  16  17  18  19  20  21
chain bonds :
6-7  7-8  8-9  14-22  18-22  27-28
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  10-11  10-15  11-12  12-13  13-14  14-15  16-17  16-
```

```
21
17-18  18-19  19-20  20-21
exact/norm bonds :
6-7  7-8  8-9  14-22  18-22  27-28
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  10-11  10-15  11-12  12-13  13-14  14-15  16-17  16-
21
17-18  18-19  19-20  20-21
isolated ring systems :
containing 1 : 10 : 16 :


G1:O,S

G2:[*1],[*2],[*3],[*4],[*5]

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:CLASS  8:CLASS  9:CLASS  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:Atom
20:Atom  21:Atom
22:CLASS  24:CLASS  25:CLASS  26:CLASS  27:CLASS  28:CLASS  29:CLASS  36:CLASS
37:Atom




L48             SCR 2043 AND 1918 AND 2050
L50        1662 SEA FILE=REGISTRY SSS FUL L47 NOT L48
L79           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L50 AND (MEDLINE/LC OR
                BIOSIS/LC OR DRUGU/LC OR EMBASE/LC)
L88        2050 SEA FILE=EMBASE ABB=ON  PLU=ON  L79
L89         605 SEA FILE=EMBASE ABB=ON  PLU=ON  L88 AND  TYROSINE KINASE?
L98          12 SEA FILE=EMBASE ABB=ON  PLU=ON  L89 AND (AY<2004 OR PY<2004 OR
                PRY<2004)


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FILE 'HCAPLUS' ENTERED AT 13:54:57 ON 16 JUL 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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PROCESSING COMPLETED FOR L54
PROCESSING COMPLETED FOR L86
PROCESSING COMPLETED FOR L98
L110          84 DUP REM L54 L86 L98 (0 DUPLICATES REMOVED)
                ANSWERS '1-64' FROM FILE HCAPLUS
                ANSWERS '65-72' FROM FILE BIOSIS
                ANSWERS '73-84' FROM FILE EMBASE

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L110 ANSWER 1 OF 84  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2007:863627  HCAPLUS  Full-text
DOCUMENT NUMBER:          147:235192
```

TITLE: Preparation of urea derivatives containing nitrogenous aromatic ring compounds as inhibitors of angiogenesis

INVENTOR(S): Funahashi, Yasuhiro; Tsuruoka, Akihiko; Matsukura, Masayuki; Haneda, Toru; Fukuda, Yoshio; Kamata, Junichi; Takahashi, Keiko; Matsushima, Tomohiro; Miyazaki, Kazuki; Nomoto, Ken-Ichi; Watanabe, Tatsuo; Obaishi, Hiroshi; Yamaguchi, Atsumi; Suzuki, Sachi; Nakamura, Katsuji; Mimura, Fusayo; Yamamoto, Yuji; Matsui, Junji; Matsui, Kenji; Yoshiba, Takako; Suzuki, Yasuyuki; Arimoto, Itaru

PATENT ASSIGNEE(S): Eisai Co., Ltd, Japan

SOURCE: U.S., 458pp., Cont.-in-part of Appl. No. PCT/JP01/09221.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 7253286	B2	20070807	US 2003-420466	20030418 <--
US 20040053908	A1	20040318		
WO 2002032872	A1	20020425	WO 2001-JP9221	20011019 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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EP 1506962	A3	20050302		
EP 1506962	B1	20080702		
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CN 101029022	A	20070905	CN 2007-10007097	20011019 <--
ES 2282299	T3	20071016	ES 2001-976786	20011019 <--
ZA 2003003567	A	20040810	ZA 2003-3567	20030508 <--
JP 2005272474	A	20051006	JP 2005-124034	20050421 <--
US 20060247259	A1	20061102	US 2005-293785	20051202 <--
US 20060160832	A1	20060720	US 2006-347749	20060203 <--
AU 2006203099	A1	20060810	AU 2006-203099	20060719 <--
AU 2006236039	A1	20061207	AU 2006-236039	20061116 <--
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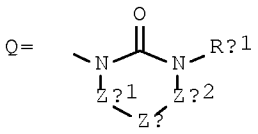
JP 2000-320420	A	20001020 <--
JP 2000-386195	A	20001220 <--
JP 2001-46685	A	20010222 <--
WO 2001-JP9221	A2	20011019 <--
AU 2001-295986	A3	20011019 <--
AU 2001-95986	TO	20011019 <--
CN 2001-819710	A3	20011019 <--
EP 2001-976786	A3	20011019 <--
JP 2002-536056	A3	20011019 <--

US 2003-420466 A3 20030418 <--
US 2005-293785 A1 20051202

OTHER SOURCE(S): MARPAT 147:235192

GI

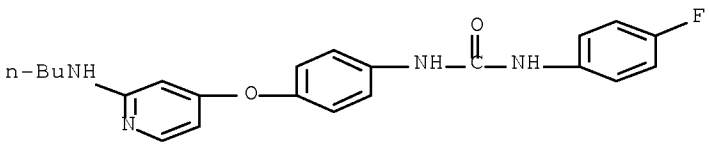


AB N-aryl or N-heteroarylurea derivs. represented by the general formula Ag-Xg-Yg-Tg1 or salts thereof, or hydrates of both [wherein Ag = (un)substituted C6-14 aryl or 5- to 14-membered heterocyclic group; Xg = single bond, O, S, C1-6 alkylene, SO, SO2, (un)substituted NH; Yg = (un)substituted C6-14 aryl, 5- to 14-membered heterocyclic group, C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl-C1-6 alkyl, 5- to 14-membered heteroaryl-C1-6 alkyl, (CH2)gSO2 (g = 1-8), (CH2)faCH:CH(CH2)fb (fa, fb = 0, 1,2,3), etc.; and Tg1 = a group of the general formula -Eg-CO-NRg1(Zg) or Q; wherein Eg = a single bond, (un)substituted NH; Rg1 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 aliphatic hydrocarbyl, etc.; Zg = C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl, etc.; Zg1, Zg2 = (a) a single bond, (b) C1-6 alkylene optionally having ≥1 atoms selected from O, S, and N in the middle or the terminus of the chain and optionally substituted with oxo, (c) (un)substituted C2-6 alkenyl] are prepared These compds. are also inhibitors of vascular endothelial growth factor receptor kinase (VEGFR2 kinase) and are useful as antitumor agents against hemangioma, pancreatic cancer, stomach cancer, colon cancer, breast cancer, prostate cancer, lung cancer, brain tumor, leukemia, or ovarian cancer, as cancer metastasis inhibitors, and for the treatment of retina neovascularization, diabetic retinopathy, atherosclerosis, or inflammatory diseases such as osteoarthritis, rheumatoid arthritis, psoriasis, or delayed hypersensitivity. Thus, to solution of 334 mg 4-[6-(4-benzyloxyphenyl)-7-(2- trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2- chlorophenylamine in 4 mL DMF were added 0.066 mL pyridine and 0.102 mL Ph chlorocarbonate and stirred at room temperature for 2.5 h to give 330 mg N-[4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea which (260 mg) was hydrogenolyzed over platinum oxide in ethanol overnight to give 160 mg N-[4-[6-(4-hydroxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H- pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea (I). I showed IC50 of 0.02 nM for inhibiting the vascular endothelial growth factor (VEGF)-stimulated sandwich tube formation in vascular endothelial cell.

IT 417714-74-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of urea derivs. containing nitrogenous aromatic ring compds. as
angiogenesis inhibitors for prevention or treatment of diseases)

RN 417714-74-0 HCAPLUS

CN Urea, N-[4-[[2-(butylamino)-4-pyridinyl]oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



INCL 546153000; 546155000; 514312000
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 27, 63

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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of urea derivs. containing nitrogenous aromatic ring compds. as
angiogenesis inhibitors for prevention or treatment of diseases)

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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of urea derivs. containing nitrogenous aromatic ring compds. as
angiogenesis inhibitors for prevention or treatment of diseases)

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of urea derivs. containing nitrogenous aromatic ring compds. as
angiogenesis inhibitors for prevention or treatment of diseases)

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of urea derivs. containing nitrogenous aromatic ring compds. as angiogenesis inhibitors for prevention or treatment of diseases)

REFERENCE COUNT: 117 THERE ARE 117 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 2 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:691680 HCAPLUS Full-text
DOCUMENT NUMBER: 147:118041
TITLE: Omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors
INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: U.S., 52pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 7235576	B1	20070626	US 2002-42203		20020111 <--
US 20030144278	A1	20030731	US 2002-283248		20021030 <--
US 20080108672	A1	20080508	US 2007-768104		20070625 <--
PRIORITY APPLN. INFO.:			US 2001-367380P	P	20010112 <--
			US 2002-42203	A1	20020111 <--

OTHER SOURCE(S): MARPAT 147:118041

AB Aryl ureas A-NHCONH-B [A, B = C5-40 (poly)aryl, optionally containing 0-4 N, O, S heteroatoms, optionally substituted by (hetero)aryl, (hetero)aryloxy, halo, cyano, nitro, alkoxy, alkylthio, amino, hydroxyalkyl, sulfo, acyl, carboxamido-groups], useful as Raf-kinase inhibitors for treatment and

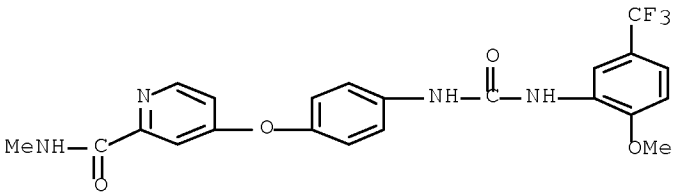
inhibition of cancerous cell growth, were prepared by standard synthetic procedures by reactions of the corresponding isocyanates with aromatic amines and tested for inhibition of Raf kinase and growth of human tumor cell lines HCT116 and DLD-1, exhibiting IC50 values of 1 nM to 10 μM. In an example, N-(4-chloro-3-trifluoromethylphenyl)-N'-[4-(2-methylaminocarbonyl- 4-pyridinyloxy)phenyl]urea was prepared by reaction of 65.9 mmol of 4-chloro-3-trifluoromethylphenyl isocyanate with 65.77 mmol of 4-(2-methylaminocarbonyl-4-pyridinyloxy)aniline in CH2Cl2 at room temperature for 22 h with 93% yield.

IT 943024-26-8P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors
for treatment and inhibition of cancerous cell growth)

RN 943024-26-8 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[2-methoxy-5-(trifluoromethyl)phenyl]amino] carbonyl]amino]phenoxy]-N-methyl-, 4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

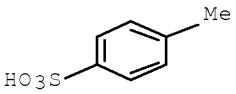
CM 1

CRN 284461-44-5
CMF C22 H19 F3 N4 O4



CM 2

CRN 104-15-4
CMF C7 H8 O3 S



INCL 514388000; 514354000; 514358000; 514597000; 514552000; 546329000; 546339000; 564054000; 564055000; 564336000
CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 63
IT 943024-26-8P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL

(Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors
for treatment and inhibition of cancerous cell growth)

IT 475207-59-1P 943024-27-9P 943024-28-0P
943024-29-1P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors
for treatment and inhibition of cancerous cell growth)

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(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors
for treatment and inhibition of cancerous cell growth)

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(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors
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4-Morpholineethanamine 2252-63-3 2524-67-6 2835-95-2 2835-99-6
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(preparation of carboxyaryl-substituted diarylureas as Raf kinase inhibitors
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L110 ANSWER 3 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1314363 HCAPLUS Full-text
DOCUMENT NUMBER: 144:57544
TITLE: Antibody drug conjugates and uses for cancer therapy
INVENTOR(S): Ebens, Allen J., Jr.; Jacobson, Frederic S.; Polakis, Paul; Schwall, Ralph H.; Sliwkowski, Mark X.; Spencer, Susan D.
PATENT ASSIGNEE(S): Genentech, Inc., USA
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US 2000-190828P P 20000321 <--
US 2000-191048P P 20000321 <--
US 2000-191314P P 20000321 <--
US 2000-193032P P 20000329 <--
US 2000-193053P P 20000329 <--
US 2000-194449P P 20000404 <--
US 2000-194647P P 20000404 <--
US 2000-195975P P 20000411 <--
US 2000-196000P P 20000411 <--
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US 2000-198121P P 20000418 <--
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US 2001-816920 B1 20010322 <--
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EP 2004-5726 A3 20010601 <--
US 2001-880457 A 20010612 <--
US 2001-882636 B1 20010614 <--
AU 2001-271938 A3 20010710 <--
AU 2001-71938 T0 20010710 <--
US 2001-927796 B1 20010809 <--
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US 2001-990711 A1 20011114 <--
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US 2002-145627 A1 20020514 <--
US 2002-145751 A 20020514 <--
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US 2002-197942 B1 20020718 <--
US 2002-199666 A1 20020718 <--
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US 2002-211858 A1 20020802 <--
AU 2002-330015 A3 20020911 <--
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AU 2003-200137 A3 20030115 <--
AU 2003-203679 A3 20030411 <--
AU 2003-261484 A 20031106 <--
US 2003-520842P P 20031117 <--
US 2003-532426P P 20031224 <--

US 2004-797366	A1	20040309
US 2004-872972	A1	20040621
US 2004-989826	A2	20041116
WO 2004-US38262	A2	20041116
AU 2005-200179	A3	20050114
US 2005-141344	A2	20050531
WO 2005-US18829	W	20050531
US 2006-461752	A2	20060801

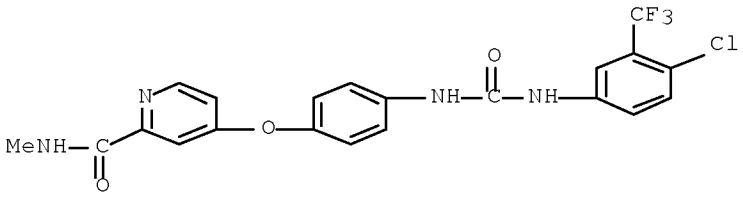
OTHER SOURCE(S): MARPAT 144:57544

AB The present invention relates to antibody-drug conjugate compds. with a formula of Ab-(L-D)p where 1 to 8 (p) maytansinoid drug moieties (D) are covalently linked by L to an antibody (Ab) which binds to an ErbB receptor, or which binds to one or more tumor-associated antigens or cell-surface receptors. These compds. may be used in methods of diagnosis or treatment of cancer, and other diseases and disorders.

IT 284461-73-0, Sorafenib
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody drug conjugates and uses for cancer therapy)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K047-48
ICS A61P035-00; G01N033-574

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 15

IT 51-21-8, 5-FU 58-05-9, Leucovorin 4856-87-5 5132-30-9 28537-70-4, 1,4-Bis-maleimidobutane 53123-88-9, Rapamycin 61825-94-3, Oxaliplatin 64987-85-5, SMCC 71865-37-7 86099-06-1 112809-51-5, Letrozole 115597-84-7 129453-61-8, Fulvestrant 179324-69-7, Bortezomib 180288-69-1, Trastuzumab 183321-74-6, Erlotinib 184475-35-2, Gefitinib 189013-00-1 193275-84-2, Lonafarnib 212142-18-2, ZK222584 216974-75-3, Bevacizumab 220127-57-1, Imatinib mesylate 231277-92-2, Lapatinib 284461-73-0, Sorafenib 557795-19-4, Sutent
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody drug conjugates and uses for cancer therapy)

L110 ANSWER 4 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:470256 HCAPLUS Full-text
DOCUMENT NUMBER: 143:20052
TITLE: Urea derivatives as kinase modulators
INVENTOR(S): Milanov, Zdravko V.; Patel, Hitesh K.; Grotzfeld, Robert M.; Mehta, Shamal A.; Andiliy, Lai G.; Lockhart, David J.
PATENT ASSIGNEE(S): Ambit Biosciences Corporation, USA

SOURCE: PCT Int. Appl., 350 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005048948	A2	20050602	WO 2004-US38288	20041115 <--
WO 2005048948	A3	20050728		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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US 20050165024	A1	20050728	US 2004-989824	20041115 <--
US 20050165074	A1	20050728	US 2004-990007	20041115 <--
US 20050171171	A1	20050804	US 2004-989766	20041115 <--
US 20050171172	A1	20050804	US 2004-989823	20041115 <--
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US 20050261315	A1	20051124	US 2004-989623	20041115 <--
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EP 1684762	A2	20060802	EP 2004-811122	20041115 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
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PRIORITY APPLN. INFO.:
US 2003-520273P P 20031113 <--
US 2003-527094P P 20031203 <--
US 2003-531082P P 20031218 <--
US 2003-531243P P 20031218 <--
WO 2004-US38288 W 20041115

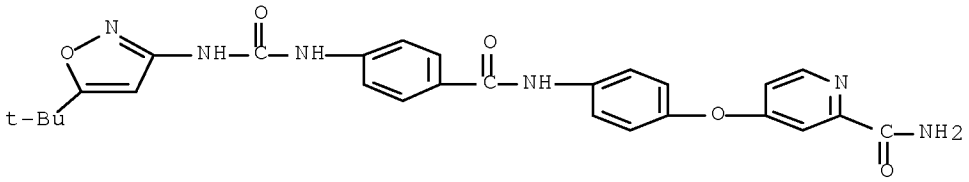
OTHER SOURCE(S): MARPAT 143:20052

AB The invention provides methods and compns. for treating conditions mediated by various kinases wherein derivs. of urea compds. are employed. The invention also provides methods of using the compds. and/or compns. in the treatment of a variety of diseases and unwanted conditions in subjects such as cellular proliferative disorders.

IT 852669-21-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urea derivs. as kinase modulators for treatment of cellular proliferative disorders)

RN 852669-21-7 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[4-[[[[5-(1,1-dimethylethyl)-3-isoxazolyl]amino]carbonyl]amino]benzoyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM A61K
CC 1-12 (Pharmacology)
Section cross-reference(s): 7, 28
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852670-49-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urea derivs. as kinase modulators for treatment of cellular proliferative disorders)

L110 ANSWER 5 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:470251 HCAPLUS Full-text
DOCUMENT NUMBER: 143:19957
TITLE: Combination therapy comprising a cyclooxygenase 2 (COX-2) inhibitor and an antineoplastic agent for treatment or prevention of neoplasia
INVENTOR(S): Masferrer, Jaime L.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 317 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005048942	A2	20050602	WO 2004-US38019	20041115 <--
WO 2005048942	A3	20060330		

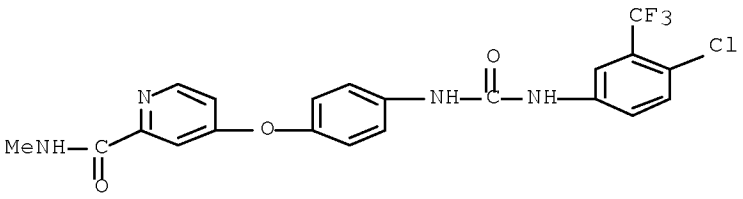
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 20050227929	A1	20051013	US 2004-989192	20041115 <--
PRIORITY APPLN. INFO.:			US 2003-519701P	P 20031113 <--

AB A method for treating or preventing neoplasia or a neoplasia-related disorder in a subject is provided, the method comprising administering to the subject an effective amount of a combination comprising a COX-2 inhibitor and an antineoplastic agent.

IT 284461-73-0, BAY 439006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K
CC 1-6 (Pharmacology)
IT 74-79-3D, L-Arginine, monomethyl derivs. 103-82-2D, Phenylacetic acid, derivs. 254-04-6D, Benzopyran, derivs. 355-25-9, NC 100100 646-08-2, β-Alethine 1400-61-9, Nystatin 1821-33-6 2353-33-5, 5-Aza-2'-deoxycytidine 5072-26-4, Buthionine sulfoximine 7689-03-4D, Camptothecin, glycoconjugate 9005-49-6, Dalteparin, biological studies 9014-42-0, RH-TPO 9074-87-7, Carboxypeptidase G2 18472-51-0, Oramed 19388-87-5, Taurolidine 33069-62-4, Paclitaxel 41941-56-4, Tocladesine 82855-09-2, Combretastatin 82952-64-5, Trimetrexate glucuronate 89778-26-7, GTx 006 97919-22-7 108560-70-9, Gallium maltolate 115427-51-5, INX-3280 118694-43-2, ILX 23-7553 128517-07-7 134774-45-1, Rasburicase 149882-10-0, Lurtotecan 152044-54-7, Epothilone B 152044-54-7D, Epothilone B, analogs 152459-95-5, Imatinib 156053-89-3, ADL 8-2698 160237-25-2, BMS-184476 162011-90-7, Rofecoxib 162635-04-3, CCI-779 169590-42-5, Celecoxib 170729-80-3, Aprepitant 172481-83-3, BMS 188797 173424-77-6, VNP-40101M 173937-91-2, Atrasentan 181695-72-7, Valdecoxib 186348-23-2, BAY 59-8862 188968-51-6, Cilengitide 191732-72-6, CDC 501 192391-48-3, Bexxar 192658-64-3 192819-27-5, CDC-801 195533-53-0, T-138067 195987-41-8 198470-84-7, Parecoxib 198470-85-8, Parecoxibsodium 198480-55-6, ERA 923 202409-33-4, Etoricoxib 205923-56-4, Cetuximab 209783-80-2, MS-275 209810-58-2, Aranesp 216503-58-1, BEC2 216974-75-3, Bevacizumab 219527-63-6, Repifermin 219989-84-1, BMS-247550 220578-59-6, Mylotarg 220991-20-8, Lumiracoxib 227619-96-7, CP-461 231277-92-2, GW-572016 236391-66-5, GTI 2040 236391-67-6, GTI 2501 246861-96-1, SB 251353 257933-82-7, EKB-569 259188-38-0, BMS-275291 261944-52-9 263351-82-2 267243-28-7 284461-73-0, BAY 439006 288392-69-8, MEDI-507 289499-45-2, CI-1033 321309-50-6, NC-100150 340014-19-9, Melacine 380907-94-8, Cytotoxin SS1(dsFv)-PE38 (synthetic) 428438-54-4, SPD 424 439153-64-7, CP 609754 447471-67-2, MG-98 543726-73-4, IMC 1C11 623174-20-9, ILX 651 791096-83-8, SD 01 845680-07-1, Lapuleucel-T 848866-33-1, T 900607 852286-49-8 852834-17-4, PK 412 852834-62-9D, TNT 1B, I131 labeled 852834-90-3, KSB 309 852834-96-9, SB 310 852835-00-8, NBI 3001 852835-01-9, APC 8020 852835-30-4, RK 0202 852835-36-0, SR 29142 852835-43-9, Stemgen 852835-52-0, ALVAC B 7.1 852835-53-1, GnRH Pharmaccine 852836-15-8, rV-MUC 1 852836-20-5, CaPVax
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor-antineoplastic agent combination for treatment or prevention of neoplasia)

L110 ANSWER 6 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:409543 HCAPLUS Full-text
DOCUMENT NUMBER: 142:457053
TITLE: Human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and

siRNA, and their use for enhancing apoptosis in cancer therapy
INVENTOR(S): Lacasse, Eric; McManus, Daniel
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042558	A1	20050512	WO 2004-CA1902	20041029 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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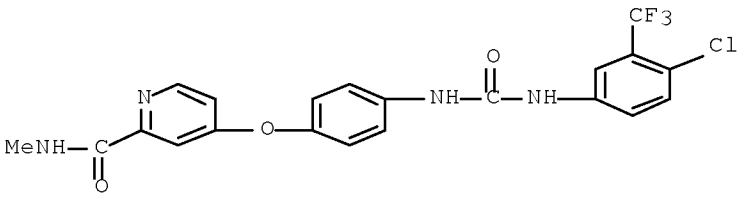
CA 2542904	A1	20050512	CA 2004-2542904	20041029 <--
EP 1682565	A1	20060726	EP 2004-789809	20041029 <--
R: DE, FR, GB				
JP 2007510408	T	20070426	JP 2006-537024	20041029 <--

PRIORITY APPLN. INFO.:			
US 2003-516192P	P	20031030 <--
WO 2004-CA1902	W	20041029

AB The invention provides nucleobase oligomers and oligonucleotide duplexes that inhibit expression of an IAP (inhibitor of apoptosis protein), and methods for using them to induce apoptosis in a cell. Specifically, the invention provides nucleic acid sequences for siRNAs and shRNAs that target human XIAP, HIAP-1 or HIAP-2 genes. The nucleobase oligomers and oligomer complexes of the present invention may also be used to form pharmaceutical compns. The invention also features methods for enhancing apoptosis in a cell by administering a nucleobase oligomer or oligomer complex of the invention in combination with a chemotherapeutic or chemosensitizing agent. RNAi sequences and vectors producing shRNA (short hairpin RNA) were transfected into HeLa cells and evaluated for their effect on XIAP, cIAP-1, or cIAP-2 protein levels. XIAP protein could also be reduced by RNAi clones in transfected breast cancer cell line MDA-MB-231. In addition, cell survival was reduced in XIAP RNAi transfected breast cancer cell line after the transfected cells were treated with TRAIL (tumor necrosis factor-related apoptosis inducing ligand).

IT 284461-73-0, BAY-43-9006
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy)
RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07H021-00
ICS A61K048-00; A61K031-7088; A61K031-713; A61P035-00; C12N015-85
CC 1-6 (Pharmacology)
Section cross-reference(s): 3, 6, 13, 14
IT 195612-80-7, Galarubicin 196488-72-9, Ranpirnase 199796-52-6, Taxoprexin 200484-11-3, CHS-828 201044-96-4, SB-T-1250 203258-60-0, Brostallicin 203923-89-1, BNP-1350 204005-46-9, SU5416 204205-90-3, D 24851 204318-14-9, Edotreotide 205923-56-4, C225 206873-63-4, Tariquidar 207862-44-0, KW-2170 209783-80-2, MS-275 209973-83-1, BLP-25 212007-18-6, Symplostatin 1 212141-54-3, Vatalanib 213819-48-8, CKD-602 216586-46-8, Virulizin 219923-05-4, ZD 6126 219989-84-1, BMS 247550 220578-59-6, Gemtuzumab zogamicin 220997-97-7, Diflomotecan 227619-96-7, CP-461 232925-18-7, Thymectacin 246252-04-0, Lutetium texaphyrin 250693-48-2, G17DT 252916-29-3, SU6668 257933-82-7, EKB-569 257938-36-6, ZD4190 259188-38-0, BMS-275291 263351-82-2, PG-TXL 267243-28-7, Canertinib 274679-00-4, Palladium bacteriopheophorbide a 284461-73-0, BAY-43-9006 284490-13-7, BCX-1777 292618-32-7, Gimatecan 305838-77-1, Neovastat 333754-36-2, DJ-927 337308-14-2, MDX-H210 339151-96-1, MDX-447 339177-26-3, ABX-EGF 342005-82-7, YM-598 343346-07-6, A 105972 349533-64-8, SB-T-101187 355113-98-3, BMS-275183 358968-10-2, 2-Des-methyldiscodermolide 358968-11-3, 19-Des-aminocarbonyldiscodermolide 358968-12-4, 2-Epidiscodermolide 373647-71-3, A 204197 387867-13-2, MLN518 393101-41-2, MAC-321 400010-39-1, SB 408075 401625-16-9, Symplostatin 3 414903-37-0, PCK-3145 437755-78-7, GW2016 439943-59-6, TLK-286 443913-73-3, ZD6474 446022-33-9, AG-2037 476172-88-0, 9(13)-Cyclodiscodermolide 492448-75-6, Oncophage 531508-98-2, GCS-100 543726-73-4, IMC-1C11 606967-38-8, MX6 623174-20-9, ILX651 623174-20-9, LU 223651 634599-18-1, WX-UK1 646067-94-9, EKB-509 665026-43-7, CV-247 674289-64-6, AP-5280 848866-30-8, GPX-100 848866-33-1, T 900607 848866-35-3, ER-86526 848866-36-4, AZ10992 848866-48-8, CA-4 848871-07-8, CBT-1 848871-42-1, CDC-394 848872-94-6, P-04 848873-95-0, Theralux 848873-96-1, PBI-1402 848873-97-2, SRL-172 848873-98-3, CDA-II 848873-99-4, SDX-101 848874-01-1, SN-4071 848874-02-2, Urocidin 849146-37-8, CTP-37 849146-41-4, Pentrix 849146-42-5, ISF-154 849148-55-6, Norelin 849148-82-9, TransMID-107 849148-97-6, MGV 849149-00-4, GMK 851343-54-9, 5-Hydroxymethyldiscodermolide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy)

L110 ANSWER 7 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:409357 HCAPLUS Full-text
DOCUMENT NUMBER: 142:457052
TITLE: Sequences of antisense IAP (inhibitor of apoptosis

protein) oligomers and their use for treatment of proliferative diseases with a chemotherapeutic agent
INVENTOR(S): Lacasse, Eric; McManus, Daniel; Durkin, Jon P.
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042030	A1	20050512	WO 2004-CA1900	20041029 <--
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2004284855	A1	20050512	AU 2004-284855	20041029 <--
CA 2542884	A1	20050512	CA 2004-2542884	20041029 <--
EP 1691842	A1	20060823	EP 2004-789807	20041029 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004015779	A	20061226	BR 2004-15779	20041029 <--
CN 1901939	A	20070124	CN 2004-80039601	20041029 <--
JP 2007509861	T	20070419	JP 2006-537023	20041029 <--
MX 2006PA04920	A	20070216	MX 2006-PA4920	20060502 <--
IN 2006MN00614	A	20070420	IN 2006-MN614	20060526 <--
NO 2006002420	A	20060731	NO 2006-2420	20060529 <--
PRIORITY APPLN. INFO.:			US 2003-516263P P	20031030 <--
			WO 2004-CA1900 W	20041029

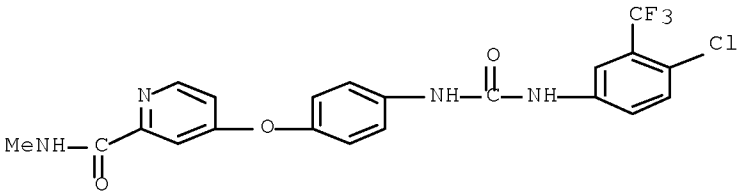
AB The invention claims the use of an antisense oligomer to human XIAP, IAP-1 or IAP-2 genes and a chemotherapeutic agent, and compns. and kits thereof, for the treatment of proliferative diseases. The invention further claims sequences for nucleobase oligomers that are antisense IAP (inhibitor of apoptosis protein) oligomers. The antisense IAP nucleobase oligomers specifically hybridize with polynucleotides encoding an IAP and reduce the amount of an IAP protein produced in a cell. Thus by reducing the IAP protein, the invention provides methods for inducing cancer cells to undergo apoptosis and for overriding anti-apoptotic signals in cancer cells. As an example of the invention, mice with s.c. H460 human lung carcinoma xenografts were injected intratumorally with XIAP antisense mixed-base 2'-O-Me RNA oligonucleotides (C5 and/or G4) and the drug vinorelbine. At the end of the 24 d treatment period, the mean relative tumor growth was reduced .apprx.70% in treated mice. The inhibition of tumor growth was correlated with down-regulation of human XIAP protein expression and an increased number of dead cells. The mice did not show any signs of cytotoxicity such as body weight loss.

IT 284461-73-0, BAY-43-9006
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with

chemotherapeutic agent)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K048-00
ICS A61K031-7088; A61P035-00; A61K031-55

CC 1-6 (Pharmacology)
Section cross-reference(s): 3, 14

IT 199796-52-6, Taxoprexin 200484-11-3, CHS-828 201044-96-4, SB-T-1250 203258-60-0, Brostallicin 203923-89-1, BNP-1350 204005-46-9, SU5416 204205-90-3, D 24851 204318-14-9, Edotreotide 205923-56-4, C225 206873-63-4, Tariquidar 207862-44-0, KW-2170 209783-80-2, MS-275 209973-83-1, BLP-25 212007-18-6, Symplostatin 1 212141-54-3, Vatalanib 213819-48-8, CKD-602 216586-46-8, Virulizin 219923-05-4, ZD 6126 219989-84-1, Azaepothilone B 220578-59-6, Gemtuzumab zogamicin 220997-97-7, Diflomotecan 227619-96-7, CP-461 232925-18-7, Thymectacin 246252-04-0, Lutetium texaphyrin 250693-48-2, G17DT 252916-29-3, SU6668 257933-82-7, EKB-569 257938-36-6, ZD4190 259188-38-0, BMS-275291 263351-82-2, PG-TXL 267243-28-7, Canertinib 274679-00-4, Palladium bacteriopheophorbide a 284461-73-0, BAY-43-9006 284490-13-7, BCX-1777 292618-32-7, Gimatecan 305838-77-1, Neovastat 333754-36-2, DJ-927 337308-14-2, MDX-H210 339151-96-1, MDX-447 339177-26-3, ABX-EGF 342005-82-7, YM-598 343346-07-6, A 105972 349533-64-8, SB-T-101187 355113-98-3, BMS-275183 358968-10-2, 2-Des-methyldiscodermolide 358968-11-3, 19-Des-aminocarbonyldiscodermolide 358968-12-4, 2-EpiDiscodermolide 373647-71-3, A 204197 387867-13-2, MLN518 393101-41-2, MAC-321 400010-39-1, SB 408075 401625-16-9, Symplostatin 3 414903-37-0, PCK-3145 437755-78-7, GW2016 439943-59-6, TLK-286 443913-73-3, ZD6474 446022-33-9, AG-2037 476172-88-0, 9(13)-Cyclodiscodermolide 492448-75-6, Oncophage 531508-98-2, GCS-100 543726-73-4, IMC-1C11 606967-38-8, MX6 623174-20-9, LU 223651 623174-20-9, ILX651 634599-18-1, WX-UK1 646067-94-9, EKB-509 665026-43-7, CV-247 674289-64-6, AP-5280 848866-30-8, GPX-100 848866-33-1, T 900607 848866-35-3, ER-86526 848866-36-4, AZ10992 848866-48-8, CA 4 848871-07-8, CBT-1 848871-42-1, CDC-394 848872-94-6, P-04 848873-95-0, Theralux 848873-96-1, PBI-1402 848873-97-2, SRL-172 848873-99-4, SDX-101 848874-01-1, SN-4071 848874-02-2, Urocidin 849146-37-8, CTP-37 849146-41-4, Pentrix 849146-42-5, ISF-154 849148-55-6, Norelin 849148-82-9, TransMID-107 849148-97-6, MGV 849149-00-4, GMK 851343-54-9, 5-Hydroxymethyldiscodermolide 851713-09-2, CDA 11 851713-35-4, 131I-TM 601
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with chemotherapeutic agent)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 8 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:346995 HCAPLUS Full-text
DOCUMENT NUMBER: 142:411371
TITLE: Preparation of pyrimidine derivatives as antitumor agents
INVENTOR(S): Dixon, Julie A.; Nagarathnam, Dhanapalan; Zhang, Lei; Wang, Chunguang; Yi, Lin; Chen, Yuanwei; Chen, Jianqing; Bear, Brian; Brands, Michael; Hillisch, Alexander; Bierer, Donald; Wang, Ming; Fu, Wenlang; Hentemann, Martin F.; Bullion, Ann-Marie
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 276 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005035507	A2	20050421	WO 2004-US33430	20041008 <--
WO 2005035507	A3	20060831		
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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EP 1689722	A2	20060816	EP 2004-809919	20041008 <--
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JP 2007508321	T	20070405	JP 2006-534438	20041008 <--
US 20050277640	A1	20051215	US 2005-78681	20050310 <--
US 20070117817	A1	20070524	US 2006-573227	20060324 <--
PRIORITY APPLN. INFO.:			US 2003-510804P P	20031010 <--
			WO 2004-US33430 W	20041008

OTHER SOURCE(S): MARPAT 142:411371
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = H, alkyl, cyclopropyl; R2 = alkyl, cyclopropyl, O-alkyl, etc.; R3 = H, halo; M = CH, N; L = carbonyl, O, (un)substituted-alkylenyl, etc.; J and Y independently = (un)substituted-aryl, -heteroaryl; A = halo, CF3, CN, etc.; m = 0-2] and their pharmaceutically acceptable salts, are prepared and disclosed as useful antitumor agents. Thus, e.g., II was prepared by etherification of 4-chloro-picoline with 4-aminophenol followed by amination of 4-chloro-6-phenylpyrimidin-2-amine (preparation given). The

cytotoxic activity of I towards HCT116 cells was evaluated and selected compds. of the invention displayed IC50 values of less than or equal to 500 nM. I should prove useful in the treatment of hyperproliferative disorders.

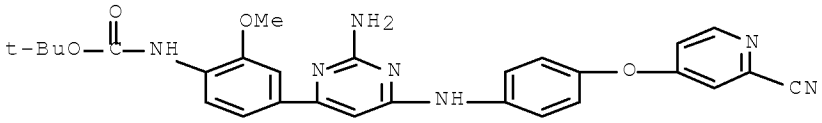
IT 850248-93-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrimidine derivs. as antitumor agents)

RN 850248-93-0 HCAPLUS

CN Carbamic acid, [4-[2-amino-6-[[4-[(2-cyano-4-pyridinyl)oxy]phenyl]amino]-4-pyrimidinyl]-2-methoxyphenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IC ICM C07D239-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

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850249-92-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidine derivs. as antitumor agents)

L110 ANSWER 9 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:283363 HCAPLUS Full-text
DOCUMENT NUMBER: 142:329832
TITLE: Combination of a vegf receptor inhibitor with a chemotherapeutic agent
INVENTOR(S): Bold, Guido; Brueggen, Josef Bernhard; Huang, Jerry Min-Jian; Kinder, Frederick Ray, Jr.; Lane, Heidi; Latour, Elisabeth Jeanne; Manley, Paul William; Wood, Jeanette Marjorie
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027972	A2	20050331	WO 2004-EP10686	20040923 <--
WO 2005027972	A3	20051103		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004273615	A1	20050331	AU 2004-273615	20040923 <--
CA 2537991	A1	20050331	CA 2004-2537991	20040923 <--
EP 1682181	A2	20060726	EP 2004-765542	20040923 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1856327	A	20061101	CN 2004-80027544	20040923 <--
BR 2004014698	A	20061128	BR 2004-14698	20040923 <--
JP 2007505938	T	20070315	JP 2006-527348	20040923 <--
MX 2006PA03163	A	20060605	MX 2006-PA3163	20060320 <--
IN 2006CN00982	A	20070615	IN 2006-CN982	20060322 <--

NO 2006001777	A	20060623	NO 2006-1777		20060421 <--
US 20080085902	A1	20080410	US 2007-573163		20070228 <--
PRIORITY APPLN. INFO.:			US 2003-505250P	P	20030923 <--
			WO 2004-EP10686	W	20040923

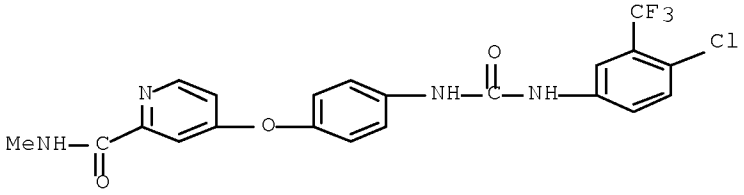
OTHER SOURCE(S): MARPAT 142:329832

AB The present invention relates to a combination therapy for treating patients suffering from proliferative diseases or diseases associated with persistent angiogenesis. The patient is treated with: (a) a VEGF inhibitor compound; and (b) one or more chemotherapeutic agents selected from the group consisting of: an aromatase inhibitor; an anti-estrogen, an anti-androgen (especially in the case of prostate cancer) or a gonadorelin agonist; a topoisomerase I inhibitor or a topoisomerase II inhibitor; a microtubule active agent, an alkylating agent, an anti-neoplastic anti-metabolite or a platin compound; a compound targeting/decreasing a protein or lipid kinase activity or a protein or lipid phosphatase activity, a further anti-angiogenic compound or a compound which induces cell differentiation processes. The patient is treated with :(a) a VEGF inhibitor compound;and (b) one or more chemotherapeutic agents selected from the group consisting of : a bradykinin 1 receptor or an angiotensin II antagonist ; a cyclooxygenase inhibitor , a bisphosphonate , a heparanase inhibitor (prevents heparan sulfate degradation) , e.g. , PI-88 , a biol. response modifier, preferably a lymphokine or interferons , e.g., interferon γ, an ubiquitination inhibitor, or an inhibitor which blocks anti-apoptotic pathways ; an inhibitor of Ras oncogenic isoforms or a farnesyl transferase inhibitor ; a telomerase inhibitor , e.g. , telomestatin ; a protease inhibitor, a matrix metalloproteinase inhibitor , a methionine aminopeptidase inhibitor , e.g. , bengamide or a derivative thereof , or a proteasome inhibitor , e. g. , PS-341. The patient is treated with : (a) a VEGF inhibitor compound (b) one or more chemotherapeutic agents selected from the group consisting of : agents used in the treatment of hematol. malignancies or FMS-like tyrosine kinase inhibitors ; an HSP90 inhibitors ; HDAC inhibitors ; mTOR inhibitors ; somatostatin receptor antagonists ; integrin antagonists ; anti-leukemic compds. ; tumor cell damaging approaches such as ionizing radiation EDG binders ; anthranilic acid amide class of kinase inhibitors ; ribonucleotide reductase inhibitors ; S-adenosylmethionine decarboxylase inhibitors ; antibodies against VEGF or VEGFR ; photodynamic therapy ; angiostatic steroids ; implants containing corticosteroids ; AT1 receptor antagonists ; ACE inhibitors.

IT 284461-73-0, BAY43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of vegf receptor inhibitor with chemotherapeutic agent)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K045-06
ICS A61K031-502

CC 1-6 (Pharmacology)
Section cross-reference(s): 63
IT 51-21-8, 5-FU 64-86-8D, Colchicine, derivs. 147-94-4, Ara-C
12772-57-5, Radicicol 30562-34-6, Geldanamycin 33515-09-2, Gonadorelin
40391-99-9, Pamidronic acid 53123-88-9, Rapamycin 75706-12-6, SU101
75747-14-7, 17AAG 107868-30-4, Exemestane 112809-51-5, Letrozole
118072-93-8, Zoledronic acid 120511-73-1, Anastrozole 120685-11-2,
PKC412 127943-53-7, Discodermolide 152459-95-5, Imatinib
159351-69-6, RAD 001 162011-90-7, Rofecoxib 162635-04-3, CCI-779
169590-42-5, Celecoxib 169944-35-8, Bisulfan 179324-69-7, PS-341
180288-69-1, Trastuzumab 181695-72-7, Valdecoxib 184475-35-2,
Gefitinib 185077-23-0, PI 88 212141-54-3 212631-79-3, PD184352
220064-45-9, GFB 111 220127-57-1, Imatinib mesylate 220991-20-8,
Lumiracoxib 252916-29-3, SU6668 260415-63-2, PD173955
284461-73-0, BAY43-9006 387867-13-2, MLN518 404950-80-7
404951-53-7 572924-54-0, AP 23573
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(combination of vegf receptor inhibitor with chemotherapeutic agent)

L110 ANSWER 10 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:283298 HCAPLUS Full-text
DOCUMENT NUMBER: 142:349042
TITLE: Combinations of chlorpromazine compounds and antiproliferative drugs for the treatment of neoplasms
INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen; Keith, Curtis
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027842	A2	20050331	WO 2004-US30368	20040916 <--
WO 2005027842	A3	20051222		
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004273910	A1	20050331	AU 2004-273910	20040916 <--
CA 2538570	A1	20050331	CA 2004-2538570	20040916 <--
EP 1670477	A2	20060621	EP 2004-788798	20040916 <--
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BR 2004014568	A	20061107	BR 2004-14568	20040916 <--
CN 1878556	A	20061213	CN 2004-80033294	20040916 <--
JP 2007505914	T	20070315	JP 2006-527024	20040916 <--
MX 2006PA03066	A	20060620	MX 2006-PA3066	20060317 <--
NO 2006001325	A	20060606	NO 2006-1325	20060323 <--

KR 2007012618 A 20070126 KR 2006-707244 20060414 <--
PRIORITY APPLN. INFO.: US 2003-504310P P 20030918 <--
WO 2004-US30368 W 20040916

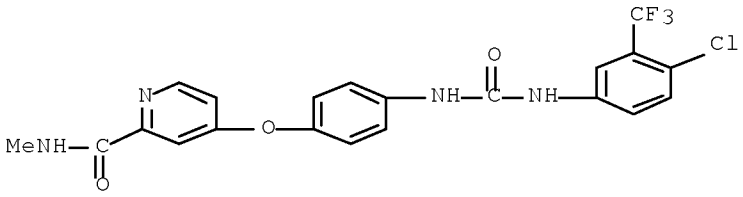
OTHER SOURCE(S): MARPAT 142:349042

AB The invention discloses a method for treating a patient having a cancer or other neoplasm by administering chlorpromazine or a chlorpromazine analog and an antiproliferative agent simultaneously or within 14 days of each other in amts. sufficient to treat the patient.

IT 284461-73-0, BAY-43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorpromazine compound-antiproliferative drug antitumor combination)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K

CC 1-6 (Pharmacology)

IT 189752-49-6, Motexafin 191732-72-6, Revimid 192185-72-1, Tipifarnib 192573-38-9, RPR 109881A 193275-84-2, Lonafarnib 195533-53-0, T 138067 195612-80-7, Galarubicin 196488-72-9, Ranpirnase 199796-52-6, Taxoprexin 200484-11-3, CHS-828 203258-60-0, Brostallicin 203923-89-1, BNP-1350 204005-46-9, SU5416 204205-90-3, D 24851 204318-14-9, Edotreotide 205923-56-4, C225 206873-63-4, Tariquidar 207862-44-0, KW-2170 209783-80-2, MS-275 212141-54-3, Vatalanib 213819-48-8, CKD-602 216586-46-8, Virulizin 219923-05-4, ZD 6126 219989-84-1, BMS 247550 220578-59-6 220997-97-7, Diflomotecan 227619-96-7, CP-461 232925-18-7, Thymectacin 246252-04-0, Lutetium texaphyrin 250693-48-2, G 17DT 252916-29-3, SU6668 257933-82-7, EKB-569 257938-36-6, ZD4190 259188-38-0, BMS-275291 263351-82-2, PG-TXL 267243-28-7, Canertinib 284461-73-0, BAY-43-9006 284490-13-7, BCX-1777 292618-32-7, Gimatecan 305838-77-1, Neovastat 337308-14-2, MDX-H 210 339151-96-1, MDX 447 339177-26-3, ABX-EGF 342005-82-7, YM-598 343346-07-6, A 105972 373647-71-3, A 204197 380610-27-5 387867-13-2, MLN518 400010-39-1, SB 408075 414903-37-0, PCK 3145 437755-78-7, GW 2016 439943-59-6, TLK-286 443913-73-3, ZD6474 446022-33-9, AG-2037 492448-75-6, Vitespen 531508-98-2, GCS 100 543726-73-4, IMC 1C11 623174-20-9 634599-18-1 646067-94-9, EKB 509 665026-43-7, CV 247 674289-64-6, AP 5280 824975-76-0, P 54 (pharmaceutical) 848866-30-8, GPX 100 848866-33-1, T 900607 848866-35-3, ER 86526 848866-36-4, AZ 10992 848866-48-8, CA 4 (pharmaceutical) 848866-48-8D, CA 4 (pharmaceutical), prodrug 848871-07-8, CBT 1 848871-42-1, CDC 394 848872-94-6, P 04 848873-95-0, Theralux 848873-96-1, PBI 1402 848873-97-2, SRL 172 848873-98-3, CDA II 848873-99-4, SDX 101 848874-01-1, SN 4071 848874-02-2, Urocidin 848874-03-3, Tyrphostin 1486 849146-37-8, CTP 37 849146-40-3, Synchrovax 849146-41-4, Pentrix 849146-42-5, ISF 154

849148-55-6, Norelin 849148-82-9, TransMID 107 849148-97-6, MGV 849149-00-4, GMK (immunomodulator)
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorpromazine compound-antiproliferative drug antitumor combination)

L110 ANSWER 11 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:182644 HCAPLUS Full-text
DOCUMENT NUMBER: 142:280215
TITLE: Preparation of heteroaryl-substituted diarylureas as tyrosine kinase inhibitors
INVENTOR(S): Hoelzemann, Guenter; Ackermann, Karl-August; Staehle, Wolfgang; Jonczyk, Alfred; Rautenberg, Wilfried; Mitjans, Francesc; Rosell-Vives, Elisabet; Adan, Jaume; Soler, Marta; Crassier, Helene
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005019192	A1	20050303	WO 2004-EP7224	20040702 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10334663	A1	20050310	DE 2003-10334663	20030730 <--
AU 2004266781	A1	20050303	AU 2004-266781	20040702 <--
CA 2533963	A1	20050303	CA 2004-2533963	20040702 <--
EP 1651626	A1	20060503	EP 2004-763077	20040702 <--
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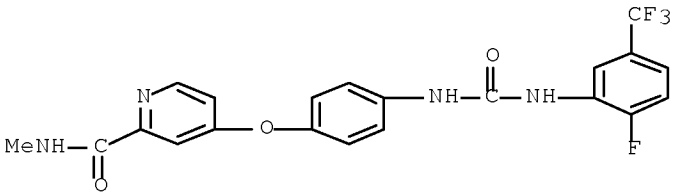
JP 2007500136	T	20070111	JP 2006-521413	20040702 <--
US 20060241301	A1	20061026	US 2006-566351	20060130 <--
PRIORITY APPLN. INFO.:			DE 2003-10334663 A	20030730 <--
			WO 2004-EP7224 W	20040702

AB Twenty-eight title compds. were claimed. Thus, 5-(4-aminophenoxy)benzo-1,2,5-thiadiazole (preparation given), 2-fluoro-5-trifluoromethylphenyl isocyanate, and Et3N were stirred in CH2Cl2 to give 1[4-(benzo-1,2,5-thiadiazol-5-yloxy)phenyl]-3-(2-fluoro-5-trifluoromethylphenyl)urea as the trifluoroacetate. The latter inhibited TIE-2 and RAF kinase with IC50 = 57 nM and 220 nM, resp.

IT 847054-10-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of heteroaryl-substituted diarylureas as tyrosine kinase inhibitors)

RN 847054-10-8 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[2-fluoro-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D285-14
ICS C07D213-81; C07D213-70; C07D319-18; C07D277-64; C07D307-86; C07D317-64; C07D213-69; C07D235-32; C07D471-04; C07D209-08; A61P035-00; A61K031-435; A61K031-4745; A61K031-4184

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 847054-10-8P 847054-11-9P 847054-12-0P 847054-13-1P
847054-14-2P 847054-15-3P 847054-16-4P 847054-18-6P 847054-20-0P
847054-22-2P 847054-24-4P 847054-26-6P 847054-28-8P 847054-30-2P
847054-31-3P 847054-32-4P 847054-33-5P 847054-34-6P 847054-35-7P
847054-36-8P 847054-37-9P 847054-38-0P 847054-39-1P 847054-40-4P
847054-41-5P 847054-42-6P 847054-43-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of heteroaryl-substituted diarylureas as tyrosine kinase inhibitors)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 12 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:141055 HCAPLUS Full-text
DOCUMENT NUMBER: 142:240466
TITLE: Preparation of piperazinylbenzocycloheptapyridines as farnesyl protein transferase inhibitors useful as antitumor agents.
INVENTOR(S): Zhu, Hugh Y.; Cooper, Alan B.; Desai, Jagdish A.; Wang, James J.-S.; Rane, Dinanath F.; Doll, Ronald J.; Njoroge, F. George; Girijavallabhan, Viyyoor M.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014577	A1	20050217	WO 2004-US25042	20040804 <--
WO 2005014577	A9	20060323		

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LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

AU 2004263493	A1	20050217	AU 2004-263493	20040804 <--
CA 2535210	A1	20050217	CA 2004-2535210	20040804 <--
US 20050059672	A1	20050317	US 2004-911340	20040804 <--
EP 1660477	A1	20060531	EP 2004-779960	20040804 <--
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BR 2004013384	A	20061017	BR 2004-13384	20040804 <--
CN 1863792	A	20061115	CN 2004-80029384	20040804 <--
JP 2007501791	T	20070201	JP 2006-522672	20040804 <--
IN 2006CN00459	A	20070518	IN 2006-CN459	20060203 <--
MX 2006PA01483	A	20060515	MX 2006-PA1483	20060207 <--
NO 2006001077	A	20060505	NO 2006-1077	20060306 <--

PRIORITY APPLN. INFO.: US 2003-493269P P 20030807 <--
US 2003-498509P P 20030828 <--
WO 2004-US25042 W 20040804

OTHER SOURCE(S): CASREACT 142:240466; MARPAT 142:240466

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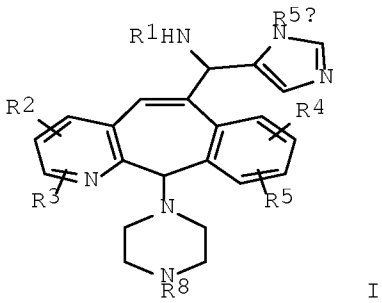

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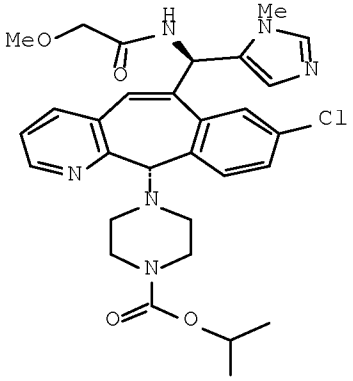


II

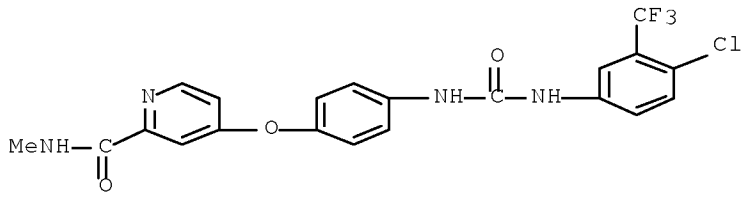
AB Title compds. [I; R1 = R9X(CR6R7)nCO, R10O2C; n = 1-6; X = O, S, N; R2-R5 = H, Br, Cl, F; R5a = H, alkyl, cycloalkyl; R6, R7 = H, alkyl; R6R7C = C3-7 cycloalkyl; R8 = R11O2C, R11SO2, R12R11aNCO, R21R22R46CO; R9 = alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, etc.; R10 = substituted aryl, heteroaryl, cycloalkyl, alkenyl, alkynyl, etc.; R11 = (substituted) alkyl, aryl, cycloalkyl, heteroaryl, heterocycloalkyl; R11a = H, OH, (substituted) alkyl, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, etc.; R12 = H, alkyl, (substituted) piperidinyl, alkylpiperidinyl; R21, R22, R46 = H, alkyl, (substituted) aryl, cycloalkyl, heteroaryl, piperidinyl, etc.], were prepared Thus, title compound (II) was prepared in several steps from 8-chloro-5,6-dihydro-11H-

benzo[5,6]cyclohepta[1,2-b]pyridin-11-one. I inhibited FPTase with IC50 in the range of <0.5 nM to 5 nM.

IT 284461-73-0, Bay 43-9006
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of piperazinylbenzocycloheptapyridines as farnesyl protein transferase inhibitors useful as antitumor agents)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D401-06
ICS C07D401-14; A61K031-415; A61P035-00

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 50-35-1, Thalidomide 566-48-3, Formestane 9034-40-6D, Lhrh, analogs 10540-29-1, Tamoxifen 15663-27-1, Cisplatin 33069-62-4, Taxol 41575-94-4, Carboplatin 53714-56-0, Leuprorelin 65807-02-5, Goserelin 84449-90-1, Raloxifene 95058-81-4, Gemcitabine 102676-47-1, Fadrozole 107868-30-4, Exemestane 112809-51-5, Letrozole 114977-28-5, Taxotere 120511-73-1, Anastrozole 129453-61-8, Fulvestrant 174722-31-7, Rituximab 179324-69-7, Bortezomib 180288-69-1, Herceptin 182167-02-8, Acolbifene 183319-69-9, Osi-774 183321-74-6, Erlotinib 184475-35-2, Iressa 190977-41-4, Genasense 204005-46-9, Su5416 205923-56-4, c225 216974-75-3, Bevacizumab 220127-57-1, Gleevec 284461-73-0, Bay 43-9006 339177-26-3, ABX-EGF 543726-73-4, IMC 1C11 543726-78-9, SU 6688
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of piperazinylbenzocycloheptapyridines as farnesyl protein transferase inhibitors useful as antitumor agents)

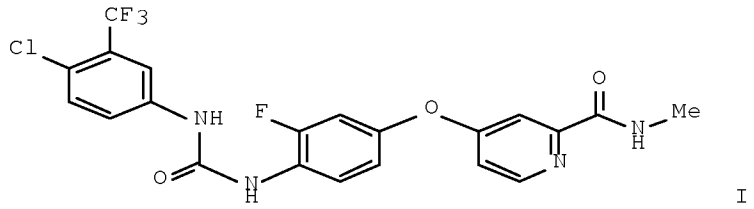
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 13 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:99470 HCAPLUS Full-text
DOCUMENT NUMBER: 142:197889
TITLE: Fluoro substituted omega-carboxyaryl diphenyl urea for treatment of raf, VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases
INVENTOR(S): Dumas, Jacques; Boyer, Stephen; Riedl, Bernd; Wilhelm, Scott
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005009961	A2	20050203	WO 2004-US23500		20040722 <--
WO 2005009961	A3	20050331			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004259760	A1	20050203	AU 2004-259760		20040722 <--
CA 2532865	A1	20050203	CA 2004-2532865		20040722 <--
US 20050038080	A1	20050217	US 2004-895985		20040722 <--
EP 1663978	A2	20060607	EP 2004-786091		20040722 <--
EP 1663978	B1	20071128			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
BR 2004012219	A	20060822	BR 2004-12219		20040722 <--
CN 1856469	A	20061101	CN 2004-80021091		20040722 <--
JP 2006528196	T	20061214	JP 2006-521221		20040722 <--
ES 2297490	T3	20080501	ES 2004-786091		20040722 <--
MX 2006PA00860	A	20060720	MX 2006-PA860		20060123 <--
IN 2006DN00402	A	20070824	IN 2006-DN402		20060123 <--
NO 2006000870	A	20060407	NO 2006-870		20060222 <--
PRIORITY APPLN. INFO.:			US 2003-489102P	P	20030723 <--
			US 2004-540326P	P	20040202
			WO 2004-US23500	W	20040722

OTHER SOURCE(S): CASREACT 142:197889

GI



I

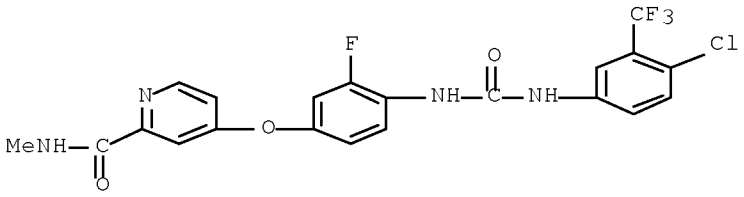
AB Title compound I is prepared I and salts thereof is prepared in several steps from 3-fluoro-4-nitrophenol, 4-chloro-N-methylpyridine-2-carboxamide and 4-chloro-3-(trifluoromethyl)phenylisocyanate. I inhibits PDGFR tyrosine kinase with IC50 = 83 nM. I is useful for the treatment of, e.g., inflammation and as an antiproliferative agent.

IT 755037-03-7P, 4-[4-[N'-(4-Chloro-3-trifluoromethylphenyl)ureido]-3-fluorophenoxy]pyridine-2-carboxylic acid methylamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(fluoro substituted omega-carboxyaryl di-Ph urea for treatment of raf, VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases)

RN 755037-03-7 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-3-fluorophenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D213-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

IT 755037-03-7P, 4-[4-[N'-(4-Chloro-3-trifluoromethylphenyl)ureido]-3-fluorophenoxy]pyridine-2-carboxylic acid methylamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(fluoro substituted omega-carboxyaryl di-Ph urea for treatment of raf, VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases)

IT 835621-07-3P 835621-08-4P 835621-09-5P
835621-10-8P, [4-[N'-(4-Chloro-3-trifluoromethylphenyl)ureido]-3-fluorophenoxy]pyridine-2-carboxylic acid amide 835621-11-9P
835621-12-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fluoro substituted omega-carboxyaryl di-Ph urea for treatment of raf, VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases)

L110 ANSWER 14 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:99357 HCAPLUS Full-text

DOCUMENT NUMBER: 142:198088

TITLE: Preparation of pyrimidinecarboxamides, pyrimidinylcarbamates and related compounds as inhibitors of T cell activation for the treatment of inflammatory diseases

INVENTOR(S): Nunes, Joseph J.; Zhu, Xiaotian; Amouzegh, Patricia; Ghiron, Chiara; Johnston, David N.; Power, Eoin Christopher

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: PCT Int. Appl., 462 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009443	A1	20050203	WO 2004-US20243	20040624 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 20050209221	A1	20050922	US 2004-875896	20040623	<--
AU 2004258862	A1	20050203	AU 2004-258862	20040624	<--
CA 2529734	A1	20050203	CA 2004-2529734	20040624	<--
EP 1648464	A1	20060426	EP 2004-777011	20040624	<--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

PRIORITY APPLN. INFO.: US 2003-482375P P 20030624 <--
US 2004-875896 A 20040623
WO 2004-US20243 W 20040624

OTHER SOURCE(S): MARPAT 142:198088

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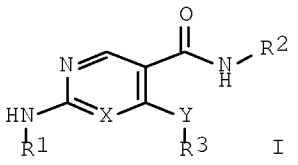

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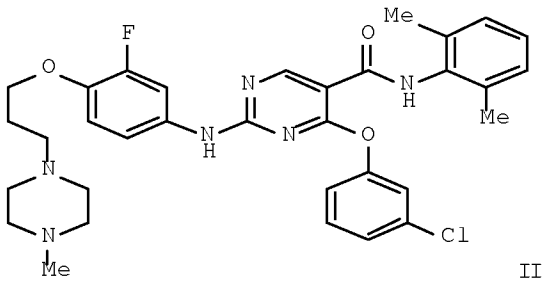
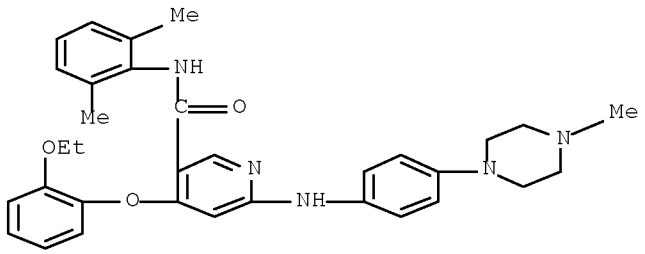


II

AB Pyrimidine and pyridine carboxamides I [wherein X = N or CH; Y = NH, O or S; R1 - R3 = certain (un)substituted monocyclic or bicyclic ring; or pharmaceutically acceptable salts thereof] as well as pyrimidinylcarbamates were prepared as inhibitors of T cell activation. For example, 2,4-dichloropyrimidine-5-carbonyl chloride, obtained by globally chlorination of uracil-5-carboxylic acid monohydrate with PCl5 in POCl3, underwent amidation with 2,6-dimethylaniline, followed by etherification with 3-chlorophenol and subsequent amination with 3-fluoro-4-(3-(4-methyl- 1-piperazinyl)propoxy)aniline to give pyrimidinecarboxamide II. Representative compds. I exhibited inhibition with IC50 values of <10 μM in the LCK-homogeneous time resolved fluorescent kinase assay. Therefore, I and pharmaceutical compns. thereof are useful in the treatment of many diseases such as inflammation.

IT 835641-38-8P, N-(2,6-Dimethylphenyl)-4-[[2-(ethyloxy)phenyl]oxy]-6-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-3-pyridinecarboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitor; preparation of pyrimidinecarboxamides and pyrimidinylcarbamates as inhibitors of T cell activation for treatment of inflammatory diseases)

RN 835641-38-8 HCAPLUS
CN 3-Pyridinecarboxamide, N-(2,6-dimethylphenyl)-4-(2-ethoxyphenoxy)-6-[[4-(4-methyl-1-piperazinyl)phenyl]amino]- (CA INDEX NAME)



IC ICM A61K031-506
ICS A61K031-505; C07D239-46; C07D239-48
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
IT 835641-38-8P, N-(2,6-Dimethylphenyl)-4-[[2-(ethyloxy)phenyl]oxy]-6-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-3-pyridinecarboxamide
835641-39-9P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-40-2P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide
835641-41-3P, 2-[[3,5-Bis(methyloxy)-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-42-4P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-(methyloxy)-4-[[2-(4-methyl-1-piperazinyl)ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-43-5P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-(methyloxy)-4-(4-methyl-1-piperazinyl)phenyl]amino]-5-pyrimidinecarboxamide 835641-44-6P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-[(difluoromethyl)oxy]-4-(4-methyl-1-piperazinyl)phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-45-7P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-chloro-4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide
835641-46-8P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[2-(methyloxy)-4-[(1-pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide 835641-47-9P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[(1-pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide
835641-48-0P 835641-49-1P, 4-[[3-(Acetylamino)phenyl]oxy]-2-[[4-(diethylamino)butyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide
835641-50-4P, 4-[[3-(Acetylamino)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-pyrimidinecarboxamide
835641-51-5P, 4-[[2-Chloro-4-(1-pyrrolidinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-52-6P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-53-7P, N-(2,6-Dimethylphenyl)-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]ami

no]-5-pyrimidinecarboxamide 835641-54-8P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-55-9P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-56-0P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-57-1P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[2-[(1-methylethyl)oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835641-58-2P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[3-[((1R)-1-methylpropyl)amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835641-59-3P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[3-[((1R)-1-methylpropyl)amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835641-60-6P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[3-[((1R)-1-methylpropyl)amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835641-61-7P 835641-62-8P 835641-63-9P, 4-[[4-[4-(Diethylamino)-4-oxobutyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-64-0P, 4-[[4-[4-(Diethylamino)-4-oxobutyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-65-1P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-[(2-pyridinyl)methyl]-5-pyrimidinecarboxamide 835641-66-2P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-[(2-pyridinyl)methyl]-5-pyrimidinecarboxamide 835641-67-3P, 2-[[3-Chloro-4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-4-[(2,2-dimethyl-2,3-dihydrobenzo[b]furan-7-yl)oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-68-4P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-4-[(2,2-dimethyl-2,3-dihydrobenzo[b]furan-7-yl)oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-69-5P, 4-[(2,2-Dimethyl-2,3-dihydrobenzo[b]furan-7-yl)oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835641-70-8P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[(2,2-dimethyl-2,3-dihydrobenzo[b]furan-7-yl)oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-71-9P, 4-[(2,2-Dimethyl-2,3-dihydrobenzo[b]furan-7-yl)oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-72-0P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-((1S)-1-phenylethyl)-5-pyrimidinecarboxamide 835641-73-1P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-((1S)-1-phenylethyl)-5-pyrimidinecarboxamide 835641-74-2P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(4-fluorophenyl)-5-pyrimidinecarboxamide 835641-75-3P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(4-fluorophenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-76-4P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2-fluorophenyl)-5-pyrimidinecarboxamide 835641-77-5P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2-fluorophenyl)-2-[[3-fluoro-4-[[3-

(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-78-6P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,4,6-trimethylphenyl)-5-pyrimidinecarboxamide 835641-79-7P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-(2,4,6-trimethylphenyl)-5-pyrimidinecarboxamide 835641-80-0P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,4,6-trifluorophenyl)-5-pyrimidinecarboxamide 835641-81-1P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-(2,4,6-trifluorophenyl)-5-pyrimidinecarboxamide 835641-82-2P, 4-[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-83-3P, 4-[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-84-4P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-4-[[4-[2-(diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-85-5P, 4-[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-86-6P, 4-[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835641-87-7P, 4-[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835641-88-8P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[2-(diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835641-89-9P, N-(2,6-Dimethylphenyl)-4-[[2-(methyloxy)-4-[3-oxo-3-(1-pyrrolidinyl)propyl]phenyl]oxy]-2-[[4-(4-methyl-1-piperazinyl)phenyl]amino]-5-pyrimidinecarboxamide 835641-90-2P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-91-3P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-92-4P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-93-5P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-94-6P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-95-7P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-96-8P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[4-[2-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835641-97-9P, 4-[[2-Chloro-4-[2-(diethylamino)ethyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-(4-methyl-1-piperazinyl)phenyl]amino]-5-pyrimidinecarboxamide 835641-98-0P, 4-[[2-Chloro-4-[2-(diethylamino)ethyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-[4-(1-methylethyl)-1-piperazinyl]phenyl]amino]-5-

pyrimidinecarboxamide 835641-99-1P, 4-[[2-Chloro-4-[2-(diethylamino)ethyl]phenyl]oxy]-2-[[4-[4-[3-(dimethylamino)propyl]-1-piperazinyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-00-7P, 2-[[4-[[[2-(Dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-propylphenyl]oxy]-5-pyrimidinecarboxamide 835642-01-8P, 2-[[3-[[[2-(Dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-propylphenyl]oxy]-5-pyrimidinecarboxamide 835642-02-9P, 2-[[4-[[[2-(Dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(ethyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-03-0P, 2-[[3-[[[2-(Dimethylamino)ethyl]amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(ethyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-04-1P, 4-[[2-Chloro-4-[2-oxo-2-(1-pyrrolidinyl)ethyl]phenyl]oxy]-2-[[4-[[[2-(diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-05-2P, 4-[[2-Chloro-4-[2-oxo-2-(1-pyrrolidinyl)ethyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-06-3P, 4-[[2-Chloro-4-[2-oxo-2-(1-pyrrolidinyl)ethyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-07-4P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[(1-pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-08-5P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[(1-pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-09-6P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[(1-pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-10-9P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-11-0P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-12-1P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-13-2P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-14-3P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-15-4P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-16-5P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[4-[[[2-(diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-17-6P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[4-[[(1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-18-7P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[[(1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-19-8P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[4-[[(1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-20-1P, N-(2,6-Dimethylphenyl)-4-[[4-[[(1-

methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-21-2P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[4-[[(1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-22-3P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-4-[[4-[[(1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-23-4P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[4-[[(1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-24-5P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[4-[[(1-methylethyl)amino]carbonyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-25-6P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[(cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-26-7P, 4-[[4-[(Cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-27-8P, 4-[[4-[(Cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-28-9P, 4-[[4-[(Cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-29-0P, 4-[[4-[(Cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-2-[[4-[[[2-(diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-30-3P, 4-[[4-[(Cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-31-4P, 4-[[4-[(Cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-32-5P, 4-[[4-[(Cyclopentylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-33-6P, 4-[[4-[2-(Diethylamino)-2-oxoethyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-34-7P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-35-8P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-36-9P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-37-0P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-38-1P, 4-[[2-Chloro-4-[[4-(1-methylethyl)-1-piperazinyl]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-39-2P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-chloro-4-[[[2-(methyloxy)ethyl]amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-40-5P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-

dimethylphenyl)-4-[[4-[3-[4-(1-methylethyl)-1-piperazinyl]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-41-6P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[4-[3-[4-(1-methylethyl)-1-piperazinyl]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-42-7P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[4-[3-[4-(1-methylethyl)-1-piperazinyl]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-43-8P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-44-9P

, 4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-45-0P, 4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-46-1P, 4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-2-[[4-[[[2-(diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-47-2P, 4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-48-3P, 4-[[2-Chloro-4-[(cyclopentylamino)carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-49-4P, 4-[[2-Chloro-4-(4-morpholinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-50-7P, 4-[[2-Chloro-4-(4-morpholinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-51-8P, 4-[[2-Chloro-4-(4-morpholinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-52-9P, 4-[[2-Chloro-4-[[(1-methylethyl)amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-53-0P, 4-[[2-Chloro-4-[[(1-methylethyl)amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-54-1P, 4-[[2-Chloro-4-[[(1-methylethyl)amino]carbonyl]phenyl]oxy]-2-[[4-[[[2-(diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-55-2P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-chloro-4-[[(1-methylethyl)amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-56-3P, N-(2,6-Dimethylphenyl)-4-[(2-ethylimidazo[1,2-a]pyridin-8-yl)oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-57-4P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-4-[[3-[3-(diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-58-5P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[3-[3-(diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-59-6P, 4-[[3-[3-(Diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-60-9P, 4-[[3-[3-(Diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide

835642-61-0P, 4-[[3-[3-(Diethylamino)-3-oxopropyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-62-1P, 4-[[2-Chloro-4-(4-morpholinylcarbonyl)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-63-2P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dichloro-4-fluorophenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-64-3P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(2,6-dichloro-4-fluorophenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-65-4P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(4-fluoro-2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-66-5P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-N-(4-fluoro-2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-67-6P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-[(5-methyl-3-isoxazolyl)methyl]-5-pyrimidinecarboxamide 835642-68-7P, 4-[[2-Chloro-4-[(diethylamino)carbonyl]phenyl]oxy]-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-N-[(5-methyl-3-isoxazolyl)methyl]-5-pyrimidinecarboxamide 835642-69-8P, 4-[[2-Chloro-4-[[[2-(methyloxy)ethyl]amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-70-1P, 4-[[2-Chloro-4-[[[2-(methyloxy)ethyl]amino]carbonyl]phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-71-2P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[(diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-72-3P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-73-4P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-2-[[4-[[[2-(diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-74-5P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[2-[4-(1-methylethyl)-1-piperazinyl]ethyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-75-6P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-76-7P, 4-[[4-[(Diethylamino)carbonyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-77-8P, 4-[[4-[3-(Cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-78-9P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[4-[3-[(1-methylethyl)amino]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-79-0P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[2-(methyloxy)-4-[3-[[2-(methyloxy)ethyl]amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-80-3P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[3-[[2-(methyloxy)ethyl]amino]-3-oxopropyl]phenyl]oxy]-5-pyrimidinecarboxamide 835642-81-4P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[4-[3-[(1-methylethyl)amino]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-

pyrimidinecarboxamide 835642-82-5P, 4-[[4-[3-(Cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-83-6P, 2-[[3,4-Bis(methyloxy)-5-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[4-[3-(cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-5-pyrimidinecarboxamide 835642-84-7P, 4-[[4-[3-(Cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-85-8P, 4-[[4-[3-(Cyclopentylamino)-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-N-(2,6-dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-5-pyrimidinecarboxamide 835642-86-9P, N-(2,6-Dimethylphenyl)-2-[[4-(3,4-dimethyl-1-piperazinyl)-3-fluorophenyl]amino]-4-[[4-[3-[(1-methylethyl)amino]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-87-0P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[4-[3-[(1-methylethyl)amino]-3-oxopropyl]-2-(methyloxy)phenyl]oxy]-5-pyrimidinecarboxamide 835642-88-1P, N-(2,6-Dimethylphenyl)-4-[[2-(methyloxy)-4-[[2-oxo-2-(1-pyrrolidinyl)ethyl]oxy]phenyl]oxy]-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-89-2P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(4-methyl-1-piperazinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-(4-morpholinyl)-2-oxoethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-90-5P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[[2-(4-morpholinyl)-2-oxoethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-91-6P, N-(2,6-Dimethylphenyl)-4-[[2-(methyloxy)-4-[[2-(4-morpholinyl)-2-oxoethyl]oxy]phenyl]oxy]-2-[[3-[[3-(1-piperidinyl)propyl]oxy]phenyl]amino]-5-pyrimidinecarboxamide 835642-92-7P, 2-[[4-[[[2-(Diethylamino)ethyl](methyl)amino]carbonyl]phenyl]amino]-N-(2,6-dimethylphenyl)-4-[[2-(methyloxy)-4-[[2-(4-morpholinyl)-2-oxoethyl]oxy]phenyl]oxy]-5-pyrimidinecarboxamide 835642-93-8P, N-(2,6-Dimethylphenyl)-2-[[3-fluoro-4-[[(1-methyl-3-piperidinyl)methyl]oxy]phenyl]amino]-4-[[2-(methyloxy)-4-[(1-pyrrolidinyl)carbonyl]phenyl]oxy]-5-pyrimidinecarboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitor; preparation of pyrimidinecarboxamides and pyrimidinylcarbamates as inhibitors of T cell activation for treatment of inflammatory diseases)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 15 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:99319 HCAPLUS Full-text
DOCUMENT NUMBER: 142:172181
TITLE: Novel targets of protein kinase-inhibiting drugs for novel disease therapies
INVENTOR(S): Biggs, William H., III; Carter, Todd; Fabian, Miles A.; Lockhart, David J.; Zarrinkar, Patrick Parvis; Treiber, Daniel Kelly; Edeen, Phillip
PATENT ASSIGNEE(S): Ambit Biosciences Corporation, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009367	A2	20050203	WO 2004-US23325	20040719 <--
WO 2005009367	A3	20050512		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

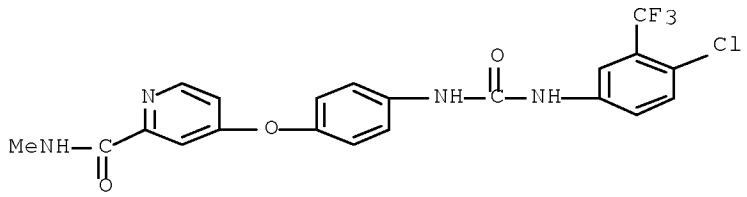
US 20060234931	A1	20061019	US 2004-894877	20040719 <--
PRIORITY APPLN. INFO.:			US 2003-488513P	P 20030717 <--

AB The invention is directed to the identification and use of addnl. targets of BIRB 796, imatinib mesylate, and BAY 43-9006. The new targets of BIRB 796, imatinib mesylate, and BAY 43-9006 can be used to screen for suitable therapeutic compds. Novel therapeutic and prophylactic uses for BIRB 796, imatinib mesylate, and BAY 43-9006 are disclosed. Protein targets of the drugs were identified using a phage-based competition assay using a panel of 69 proteins including 48 kinases.

IT 284461-73-0, BAY 43-9006
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel targets of protein kinase-inhibiting drugs for novel disease therapies)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K

CC 7-4 (Enzymes)
Section cross-reference(s): 1, 3

IT 220127-57-1, Imatinib mesylate 284461-73-0, BAY 43-9006
285983-48-4, BIRB 796
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel targets of protein kinase-inhibiting drugs for novel disease therapies)

L110 ANSWER 16 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:55204 HCAPLUS Full-text
DOCUMENT NUMBER: 142:134581

TITLE: Preparation of malonamide derivatives useful as raf-kinase inhibitors

INVENTOR(S): Bruge, David; Buchstaller, Hans-Peter; Wiesner, Matthias; Finsinger, Dirk; Baumgarth, Manfred; Sirrenberg, Christian; Zenke, Frank; Amendt, Christiane; Grell, Matthias

PATENT ASSIGNEE(S): Merck Patent GmbH, Germany

SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

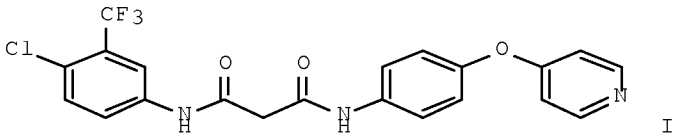
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005005389	A2	20050120	WO 2004-EP6573	20040618 <--
WO 2005005389	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004255566	A1	20050120	AU 2004-255566	20040618 <--
CA 2531485	A1	20050120	CA 2004-2531485	20040618 <--
EP 1641759	A2	20060405	EP 2004-740026	20040618 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2007508238	T	20070405	JP 2006-518009	20040618 <--
US 20070213374	A1	20070913	US 2007-563830	20070125 <--

PRIORITY APPLN. INFO.: EP 2003-14556 A 20030707 <--
WO 2004-EP6573 W 20040618

OTHER SOURCE(S): MARPAT 142:134581

GI



I

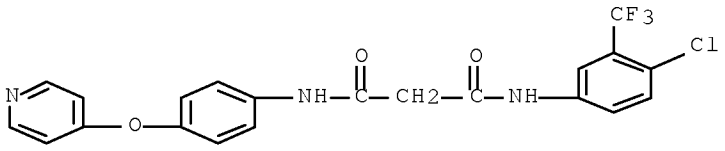
AB Malonamide derivs. of formula A-D-B [wherein: D is (un)substituted bivalent malonamide moiety; A and B are independently selected from (hetero)aryl derivs.], useful as raf-kinase inhibitors (no biol. data), were prepared For instance, malonamide derivative I was obtained via amidation of 3-[(4-chloro-3-trifluoromethylphenyl)amino]-2-oxo-propionic acid by 4-(4-pyridinyloxy)phenylamine with a yield of 57%.

IT 827029-05-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of malonamide derivs. useful as raf-kinase inhibitors)

RN 827029-05-0 HCAPLUS
CN Propanediamide, N1-[4-chloro-3-(trifluoromethyl)phenyl]-N3-[4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)



IC ICM C07D213-00
CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 27, 63
IT 827029-05-0P 827029-06-1P 827029-07-2P 827029-08-3P
827029-09-4P 827029-10-7P 827029-11-8P 827029-22-1P
827029-23-2P 827029-24-3P 827029-25-4P
827029-26-5P 827029-27-6P 827029-28-7P
827029-29-8P 827029-30-1P 827029-31-2P
827029-32-3P 827029-33-4P 827029-34-5P
827029-35-6P 827029-36-7P 827029-37-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of malonamide derivs. useful as raf-kinase inhibitors)

L110 ANSWER 17 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:14200 HCAPLUS Full-text
DOCUMENT NUMBER: 142:86701
TITLE: Diaryl ureas for treatment of diseases mediated by PDGFR
INVENTOR(S): Wilhelm, Scott; Dumas, Jacques; Ladouceur, Gaetan; Lynch, Mark; Scott, William J.
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000284	A2	20050106	WO 2004-US15653	20040519 <--
WO 2005000284	A3	20050310		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2526636	A1	20050106	CA 2004-2526636		20040519 <--
US 20050059703	A1	20050317	US 2004-848567		20040519 <--
EP 1626714	A2	20060222	EP 2004-776037		20040519 <--
EP 1626714	B1	20070704			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

JP 2006528986	T	20061228	JP 2006-533210		20040519 <--
AT 366108	T	20070715	AT 2004-776037		20040519 <--
ES 2288694	T3	20080116	ES 2004-776037		20040519 <--
AT 384264	T	20080215	AT 2004-752642		20040519 <--
MX 2005PA12486	A	20060703	MX 2005-PA12486		20051118 <--
PRIORITY APPLN. INFO.:			US 2003-471735P	P	20030520 <--
			US 2003-520399P	P	20031117 <--
			US 2004-556062P	P	20040325
			WO 2004-US15653	W	20040519

OTHER SOURCE(S): MARPAT 142:86701

AB The present invention provides methods for treating and/or preventing conditions and diseases in humans and other mammals that are associated with and/or mediated by signal transduction pathways comprising platelet-derived growth factor receptor (PDGFR), especially PDGFR-β, by administering diaryl ureas. The present invention also provides devices and methods for treating, ameliorating, preventing, or modulating restenosis following angioplastic surgery or other invasive procedures that affect or injure the vascular system, and graft rejection following transplantation of a donor tissue into a host, where a stent or other implantable device comprises an effective amount of diaryl ureas. For example, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N- methylcarbamoyl)-4-pyridyloxy]phenyl] urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]-2-fluorophenyl] urea, and N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]-2-chl orophenyl]urea showed an IC50 of less than 10 μM in a pPDGFR-β sandwich ELISA in AoSMC cells.

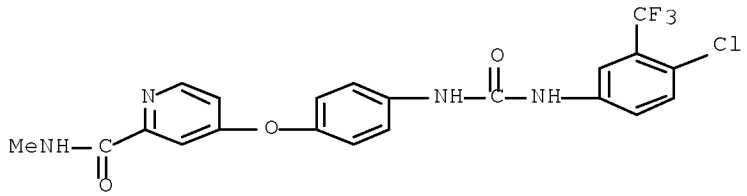
IT 284461-73-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(diaryl ureas for prevention and/or treatment of diseases mediated by platelet-derived growth factor receptor)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-00

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

IT 57-13-6D, Urea, diaryl derivs. 284461-73-0 284461-74-1 284461-80-9 284462-18-6 284462-19-7

475207-59-1 583840-03-3 583840-04-4
755037-03-7 755037-03-7D, salts 755037-04-8
757229-80-4 819792-84-2 819792-85-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diaryl ureas for prevention and/or treatment of diseases mediated by platelet-derived growth factor receptor)

L110 ANSWER 18 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1313901 HCAPLUS Full-text
DOCUMENT NUMBER: 144:51598
TITLE: Preparation of amino-substituted pyrimidines as antitumor agents
INVENTOR(S): Dixon, Julie A.; Nagarathnam, Dhanapalan; Zhang, Lei; Wang, Chunguang; Yi, Lin; Chen, Yuanwei; Chen, Jianqing; Bear, Brian R.; Brands, Michael; Hillisch, Alexander; Bierer, Donald; Wang, Ming; Fu, Wenlang; Hentemann, Martin F.; Bullion, Ann-Marie; Patel, Manoj
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 182 pp., Cont.-in-part of Appl. No. PCT/US04/033430.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050277640	A1	20051215	US 2005-78681	20050310 <--
WO 2005035507	A2	20050421	WO 2004-US33430	20041008 <--
WO 2005035507	A3	20060831		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-510804P P 20031010 <--
WO 2004-US33430 A2 20041008
OTHER SOURCE(S): CASREACT 144:51598; MARPAT 144:51598
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = H, alkyl, cyclopropyl; R2 = alkyl, cyclopropyl, O-alkyl, etc.; R3 = H, halo; M = CH, N; L = carbonyl, O, (un)substituted alkylenyl, etc.; J and Y independently = substituted aryl, heteroaryl; A = halo, CF3, CN, etc.; m = 0-2] and their pharmaceutically acceptable salts, are prepared and disclosed as useful antitumor agents. Thus, coupling 6-chloro-N4-(4-{[2-(trifluoromethyl)pyridin-4-yl]oxy}phenyl)pyrimidine-2,4- diamine with 1,3-

dimethylphenylboronic acid afforded 56% II which showed IC50 of 62 nM in test for cytotoxic activity on HCT-116 cells.

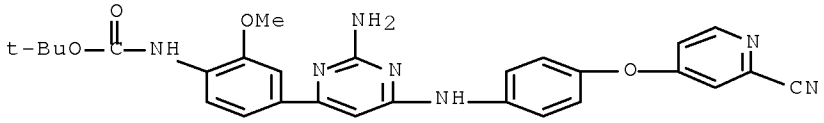
IT 850248-93-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino-substituted pyrimidines as antitumor agents)

RN 850248-93-0 HCAPLUS

CN Carbamic acid, [4-[2-amino-6-[[4-[(2-cyano-4-pyridinyl)oxy]phenyl]amino]-4-pyrimidinyl]-2-methoxyphenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IC ICM A61K031-5377

ICS A61K031-506; C07D413-14; C07D043-02

INCL 514235500; 514252140; 514256000; 544122000; 544295000; 544296000; 544329000

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

IT 850246-99-0P 850247-00-6P 850247-01-7P 850247-02-8P 850247-03-9P
850247-04-0P 850247-05-1P 850247-07-3P 850247-08-4P 850247-09-5P
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850249-92-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino-substituted pyrimidines as antitumor agents)

L110 ANSWER 19 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:735326 HCAPLUS Full-text
DOCUMENT NUMBER: 143:229730
TITLE: Preparation of tetrahydroisoquinoline derivatives for treating diseases mediated by protein trafficking or chloride channel activity
INVENTOR(S): Pregel, Marko J.; Hirth, Bradford H.; Kane, John L.; Qiao, Shuang; Gregory, Jill; Cuff, Lisa
PATENT ASSIGNEE(S): Genzyme Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 52 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050176761	A1	20050811	US 2004-6042	20041207 <--
PRIORITY APPLN. INFO.:			US 2003-531873P P	20031223 <--

OTHER SOURCE(S): CASREACT 143:229730; MARPAT 143:229730
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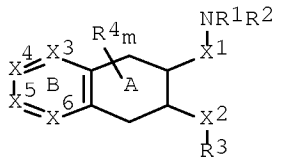


I

AB Tetrhydroisoquinoline derivs. I (variables defined below), pharmaceutical compns. comprising them and methods of treating disease are disclosed herein.

The disclosed compds. are useful in the treatment and prevention of diseases mediated by chloride channel activity and/or protein trafficking, including, but not limited to, diseases associated with impaired mucociliary clearance such as cystic fibrosis, bronchitis, emphysema, and the like. For I the variables are: X1 = CH2, CO, SO, SO2; X2 = CH2, CO, COCH2, CO2, COS, O, S, SO; X3, X4, X5, X6 = N, CH, wherein at least 1 of X3, X4, X5, X6 = CH; Ring B is optionally substituted in any substitutable carbon; R1 and R2 = H or an optionally substituted aliphatic, aryl, heteroaryl, heterocyclic, cycloalkyl, peptide, or amino acid group, provided that R1 and R2 are not both H; or, R1 and R2, taken together with the nitrogen to which they are bonded, are an optionally substituted heterocyclic group; R3 = optionally substituted aryl, heteroaryl, cycloalkyl, or heterocyclic group; m = 0-2; each R4 = halogen, OH, SH, Ra, ORa, SRa, NH2, NHRa, NRa2, C(O)NRa2, CF3, CN, or NO2; and Ra = C1-C5 branched or linear alkyl group.

IT 851777-89-4P

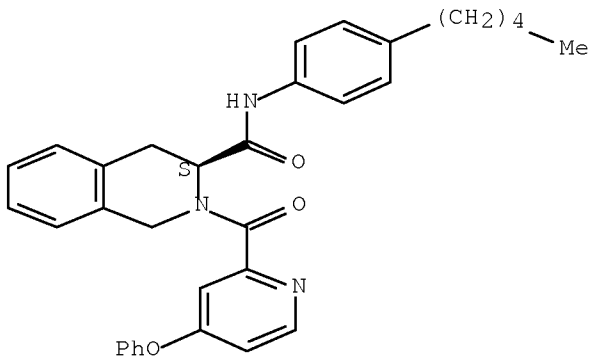
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of tetrahydroisoquinoline derivs. for treating diseases mediated by protein trafficking or chloride channel activity)

RN 851777-89-4 HCAPLUS

CN 3-Isoquinolinecarboxamide, 1,2,3,4-tetrahydro-N-(4-pentylphenyl)-2-[(4-phenoxy-2-pyridinyl)carbonyl]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-4709
ICS A61K031-47

INCL 514310000

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT 851777-43-0P 851777-46-3P 851777-47-4P 851777-48-5P 851777-49-6P
851777-50-9P 851777-52-1P 851777-53-2P 851777-54-3P,
2-(3-Phenoxybenzoyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid
N-(4-heptylphenyl)amide 851777-55-4P 851777-56-5P 851777-57-6P
851777-59-8P 851777-60-1P 851777-61-2P 851777-62-3P 851777-63-4P,
(S)-2-(3-Phenoxybenzoyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid
N-(6-pentylpyridin-3-yl)amide 851777-64-5P 851777-66-7P 851777-67-8P
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851777-77-0P 851777-79-2P 851777-80-5P 851777-81-6P 851777-83-8P
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851777-90-7P 851777-91-8P 851777-92-9P 851777-93-0P,
(S)-2-[[5-(Cyclohexyloxy)pyridin-3-yl]carbonyl]-1,2,3,4-

tetrahydroisoquinoline-3-carboxylic acid N-(4-pentylphenyl)amide 851777-94-1P 851777-95-2P, (S)-2-(2-Isopropoxypyridine-4-carbonyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (4-pentylphenyl)amide 862504-12-9P 862504-13-0P 862504-14-1P 862504-15-2P 862504-16-3P 862504-17-4P 862504-18-5P 862504-19-6P 862504-20-9P 862504-21-0P 862504-22-1P 862504-23-2P 862504-24-3P, 2-[(Naphthalen-2-yl)carbonyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid N-(4-chlorophenyl)amide 862504-25-4P 862504-26-5P 862504-27-6P 862504-28-7P 862504-29-8P 862504-30-1P 862504-31-2P 862504-32-3P 862504-33-4P 862504-34-5P 862504-35-6P 862504-36-7P 862504-37-8P 862504-38-9P 862504-39-0P 862504-40-3P 862504-41-4P 862504-42-5P 862504-43-6P 862504-44-7P 862504-45-8P 862504-46-9P 862504-47-0P 862504-48-1P 862504-49-2P 862504-50-5P 862504-51-6P 862504-52-7P 862504-53-8P 862504-54-9P 862504-55-0P 862504-56-1P 862504-57-2P 862504-58-3P 862504-59-4P 862504-60-7P 862504-61-8P 862504-62-9P 862504-63-0P 862504-64-1P 862504-65-2P 862504-66-3P 862504-67-4P 862504-68-5P 862504-69-6P 862504-70-9P 862504-71-0P 862504-72-1P 862504-73-2P 862504-74-3P 862504-75-4P, 2-(3-Phenoxybenzoyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid [2-(4-bromophenyl)ethyl]amide 862504-78-7P 862504-81-2P 862504-84-5P 862504-87-8P 862504-90-3P 862504-93-6P 862504-96-9P 862504-99-2P 862505-04-2P 862505-09-7P 862505-12-2P 862505-21-3P, 2-(3-Phenoxybenzoyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid N-[4-[(acetyl)(hexyl)amino]phenyl]amide 862505-24-6P 862505-33-7P, 2-(3-Phenoxybenzoyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid N-[4-(butyrylmethylamino)phenyl]amide 862505-42-8P 862505-45-1P 862505-52-0P 862505-57-5P 862505-64-4P 862505-65-5P 862505-68-8P 862505-71-3P 862505-74-6P 862505-77-9P 862505-80-4P 862505-85-9P 862505-96-2P, (S)-2-[4-Ethoxy-3-phenoxy-benzoyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid N-(4-pentylphenyl)amide 862506-01-2P 862506-10-3P 862506-13-6P, (S)-2-[4-Methoxy-3-[2-(morpholin-4-yl)ethoxy]benzoyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid N-(4-pentylphenyl)amide 862506-24-9P 862506-29-4P 862506-32-9P 862506-34-1P 862506-36-3P 862506-38-5P 862506-41-0P 862506-44-3P 862506-47-6P 862506-52-3P 862506-57-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of tetrahydroisoquinoline derivs. for treating diseases mediated by protein trafficking or chloride channel activity)

L110 ANSWER 20 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:641861 HCAPLUS Full-text
DOCUMENT NUMBER: 143:146651
TITLE: JAK/STAT inhibitors and MAPK/ERK inhibitors for respiratory syncytial virus (RSV) infection
INVENTOR(S): Mohapatra, Shyam S.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 46 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20050159385	A1	20050721	US 2004-18954		20041220 <--
PRIORITY APPLN. INFO.:			US 2003-531052P	P	20031219 <--

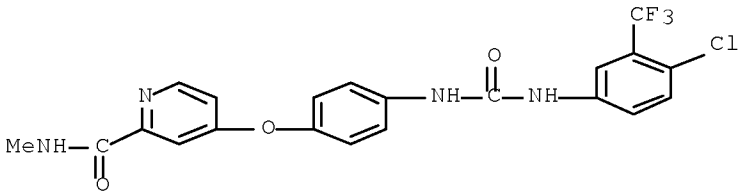
AB The invention discloses a method for treating or reducing the likelihood of developing a RSV infection in a subject by administering an effective amount

of an inhibitor of the janus kinase (JAK)/signal transducer and activator of transcription (STAT) signaling pathway or the mitogen-activated kinase (MAPK)/extracellular signal-regulated kinase (ERK1/2) signaling pathway to the subject. Also disclosed is a pharmaceutical composition that includes an inhibitor of JAK/STAT or MAPK/ERK signaling to the subject; and a pharmaceutically acceptable carrier. Further disclosed is a method for identifying agents useful for treating or reducing the likelihood of developing an RSV infection.

IT 284461-73-0, BAY 43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(JAK/STAT inhibitors and MAPK/ERK inhibitors for respiratory syncytial virus infection treatment)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K048-00
ICS A61K039-395; A61K038-17

INCL 514044000; 514002000; 424146100

CC 1-5 (Pharmacology)

IT 4959-60-8, 4,5-Dimethoxy-2-nitrobenzamide 4998-07-6, 4,5-Dimethoxy-2-nitrobenzoic acid 21561-09-1 28822-58-4, IBMX 66575-29-9, Forskolin 109511-58-2, U0126 133550-30-8, AG490 167869-21-8, PD98059 177075-18-2, ISIS 5132 201653-76-1 202475-60-3, 4-4'-Hydroxyphenylamino-6,7-dimethoxyquinazoline 210419-07-1, Ro 09-2210 211555-04-3 212631-79-3, PD184352 220904-83-6, GW5074 284461-73-0, BAY 43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(JAK/STAT inhibitors and MAPK/ERK inhibitors for respiratory syncytial virus infection treatment)

L110 ANSWER 21 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:469894 HCAPLUS Full-text

DOCUMENT NUMBER: 143:7592

TITLE: Preparation of arylpyrrolecarboxamides as Raf kinase inhibitors for treatment of tumors.

INVENTOR(S): Finsinger, Dirk; Buchstaller, Hans-Peter; Burgdorf, Lars; Wiesner, Matthias; Amendt, Christiane; Grell, Matthias; Sirrenberg, Christian; Zenke, Frank

PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany

SOURCE: Ger. Offen., 32 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10354060	A1	20050602	DE 2003-10354060	20031119 <--
AU 2004291255	A1	20050602	AU 2004-291255	20041026 <--
CA 2546334	A1	20050602	CA 2004-2546334	20041026 <--
WO 2005049603	A1	20050602	WO 2004-EP12076	20041026 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1685125	A1	20060802	EP 2004-790859	20041026 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1882571	A	20061220	CN 2004-80034345	20041026 <--
BR 2004016690	A	20070130	BR 2004-16690	20041026 <--
JP 2007511553	T	20070510	JP 2006-540216	20041026 <--
IN 2006KN00936	A	20070420	IN 2006-KN936	20060417 <--
MX 2006PA05478	A	20060811	MX 2006-PA5478	20060515 <--
US 20070149594	A1	20070628	US 2006-579825	20060517 <--
PRIORITY APPLN. INFO.:			DE 2003-10354060 A	20031119 <--
			WO 2004-EP12076 W	20041026

OTHER SOURCE(S): MARPAT 143:7592

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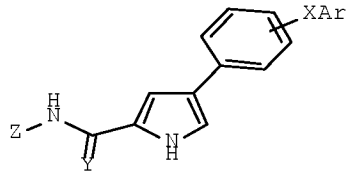


I

AB Title compds. [I; Ar = (substituted) Ph, naphthyl, biphenyl, heterocyclyl; X = O, S, (CH2)n, CO, (CH2)nO, (CH2)nNH, etc.; n = 1-3; Y = O, S, CHNO2, C(CN)2, NR4; R4 = H, cyano, OH, etc.; Z = Ar, ArXAr, CH2Ar, CH2ArXAr; Ar = (substituted) Ph], were prepared as Raf kinase inhibitors (no data). Thus, 4-(PhCH2O)C6H4CH2CO2H, DMF, and POCl3 were heated together at 70° for 4 h followed by cooling and addition of ice water and aqueous NaClO4 to give 98% [2-(4-benzyloxyphenyl)-3-dimethylaminoallylidene]dimethylammonium perchlorate. This was refluxed 24 h with glycine Et ester hydrochloride in EtOH containing 20% NaOEt to give 91% Et 4-(4-benzyloxyphenyl)-1H-pyrrole-2- carboxylate. Hydrogenolysis of the latter in EtOAc over Pd/C gave 91% Et 4-(4-hydroxyphenyl)-1H-pyrrole-2-carboxylate. This was heated with 4-chloropyridine-2-carboxylic acid N-methylamide at 160° for 48 h to give 40% Et 4-[4-(2-methylcarbamoylpyridin-4-yloxy)phenyl]-1H-pyrrole-2- carboxylate. Saponification with 2N NaOH in EtOH at 60° for 16 h followed by acidification

with HCl gave 85% free acid, which was stirred 48 h in DMF with 5-amino-2-chlorobenzotrifluoride, N-(3-dimethylaminopropyl)-N'- ethylcarbodiimide hydrochloride, and 1-hydroxybenzotriazole hydrate to give 17% 4-[4-[5-(4-chloro-3-trifluoromethylphenylcarbamoyl)-1H-pyrrol-3- yl]phenoxy]pyridine-2-carboxylic acid N-methylamide.

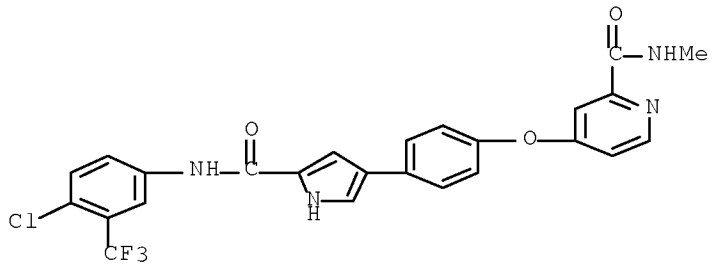
IT 852455-19-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of arylpyrrolecarboxamides as Raf kinase inhibitors for treatment of tumors)

RN 852455-19-7 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[5-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]-1H-pyrrol-3-yl]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D401-12

ICS A61K031-4439; A61P035-00; A61P017-00; A61P019-00; A61P031-00; A61P013-00; A61P037-00

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT 852455-19-7P 852455-20-0P 852455-21-1P 852455-22-2P 852455-23-3P 852455-24-4P 852455-25-5P 852455-26-6P 852455-27-7P 852455-28-8P 852455-29-9P 852455-30-2P 852455-31-3P 852455-32-4P 852455-33-5P 852455-34-6P 852455-35-7P 852455-36-8P 852455-37-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of arylpyrrolecarboxamides as Raf kinase inhibitors for treatment of tumors)

L110 ANSWER 22 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:1154653 HCAPLUS Full-text

DOCUMENT NUMBER: 142:93545

TITLE: Preparation of diaryl ureas with kinase inhibiting activity

INVENTOR(S): Wilhelm, Scott; Dumas, Jacques; Ladouceur, Gaetan; Lynch, Mark; Scott, William J.

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2004113274	A2	20041229	WO 2004-US15655		20040519	<--
WO 2004113274	A3	20050303				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW						
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG						
CA 2526617	A1	20041229	CA 2004-2526617		20040519	<--
US 20050059703	A1	20050317	US 2004-848567		20040519	<--
EP 1636585	A2	20060322	EP 2004-752642		20040519	<--
EP 1636585	B1	20080116				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK						
JP 2007511203	T	20070510	JP 2006-533211		20040519	<--
AT 366108	T	20070715	AT 2004-776037		20040519	<--
ES 2288694	T3	20080116	ES 2004-776037		20040519	<--
AT 384264	T	20080215	AT 2004-752642		20040519	<--
MX 2005PA12491	A	20060929	MX 2005-PA12491		20051118	<--
US 20070020704	A1	20070125	US 2006-571100		20060728	<--
PRIORITY APPLN. INFO.:			US 2003-471735P	P	20030520	<--
			US 2003-520399P	P	20031117	<--
			US 2004-556062P	P	20040325	
			WO 2004-US15655	W	20040519	

OTHER SOURCE(S): MARPAT 142:93545
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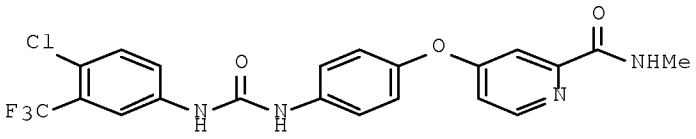


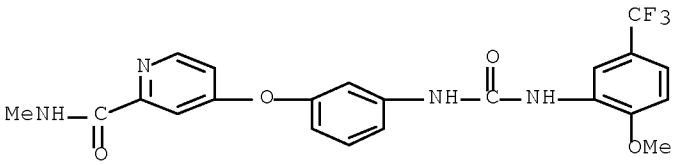
I

AB Diaryl ureas B-NH-CO-NH-L-(CH2)m-X-(CH2)p-L1-(Q)1-3 [I; B = (un)substituted Ph, naphthyl, or heteroaryl; L, =(un)substituted Ph, naphthyl, or heteroaryl; X = bond, O, CO, NR3, NR3CO, S, CONR3, CF2, CCl2, CHF, CH(OH), C.tplbond.C, CH:CH, CR4R5; m, p = independently 0-4; L1 = any group L, 5-6 membered cyclic structure; Q = independently COR4, CO2R4, CONR4R5; each R3-R5 = independently H, (un)substituted C1-5 alkyl,C3-5 cycloalkyl, Ph, C1-3 alkylphenyl, C0-4 alkylheteroaryl], useful to treat diseases and conditions associated with signal transduction pathways comprising of at least one of raf, VEGFR, PDGFR, p38 and/or FLT-3. E.g., a multi-step synthesis of the urea II which produced dose-dependent 45-68% inhibition of tumor growth in a staged HCT 116 colon (mutant k-Ras) xenograft model.

IT 284461-42-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diaryl ureas with kinase inhibiting activity)

RN 284461-42-3 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[3-[[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07C273-18
CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 63
IT 228418-48-2P 284461-33-2P 284461-34-3P 284461-35-4P 284461-36-5P
284461-37-6P 284461-38-7P 284461-39-8P 284461-40-1P 284461-41-2P
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284462-35-7P 284462-36-8P 284462-70-0P 755037-03-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diaryl ureas with kinase inhibiting activity)

L110 ANSWER 23 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:965067 HCAPLUS Full-text
DOCUMENT NUMBER: 141:406039
TITLE: Combinations for the treatment of diseases involving cell proliferation, migration or apoptosis of myeloma

cells, or angiogenesis

INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin Friedrich; Baum, Anke; Munzert, Gerd; Van Meel, Jacobus C. A.

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.

SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096224	A2	20041111	WO 2004-EP4363	20040424 <--
WO 2004096224	A3	20041216		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1473043	A1	20041103	EP 2003-9587	20030429 <--
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AU 2004233576	A1	20041111	AU 2004-233576	20040424 <--
CA 2523868	A1	20041111	CA 2004-2523868	20040424 <--
EP 1622619	A2	20060208	EP 2004-729366	20040424 <--
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BR 2004009919	A	20060425	BR 2004-9919	20040424 <--
JP 2006524634	T	20061102	JP 2006-500099	20040424 <--
MX 2005PA11656	A	20051215	MX 2005-PA11656	20051028 <--
NO 2005005605	A	20051128	NO 2005-5605	20051128 <--

PRIORITY APPLN. INFO.:			
EP 2003-9587	A	20030429	<--
EP 2004-508	A	20040113	
EP 2004-1171	A	20040121	
WO 2004-EP4363	W	20040424	

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepns. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

IT 284461-73-0, BAY-43-9006

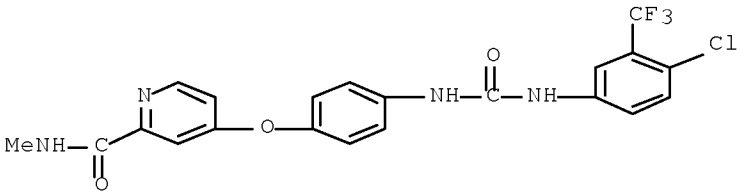
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug combinations for diseases involving cell proliferation and migration or apoptosis or angiogenesis including protein tyrosine

kinase receptor antagonists and radiotherapy)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-496
ICS A61K031-517; A61P035-00

CC 1-6 (Pharmacology)
Section cross-reference(s): 8, 15

IT 183321-74-6, Erlotinib 183552-38-7, Abarelix 184475-35-2, Gefitinib 185243-69-0, Etanercept 187724-61-4, PKI-166 190977-41-4, Oblimersen 191732-72-6, Revimid 204005-46-9, SU-5416 205923-56-4, Cetuximab 206181-63-7, Ibritumomab 212141-54-3, Vatalanib 213327-37-8, Oregovomab 215369-21-4, DC 101 216503-57-0, Alemtuzumab 216503-58-1, Mitumomab 216974-75-3, Avastin 252003-65-9, CP-547632 252916-29-3, SU-6668 257933-82-7, EKB-569 262367-70-4 263338-11-0 267227-08-7, Apolizumab 284461-73-0, BAY-43-9006 288383-20-0 289499-45-2, CI-1033 305838-77-1, Neovastat 319460-85-0 334949-28-9 334949-30-3 334949-31-4 334949-32-5 334949-38-1 334950-47-9 339186-68-4, EMD-72000 402857-58-3, CEP-7055 437755-78-7, GW 2016 439081-18-2 439943-59-6, TLK-286 443913-73-3 444731-52-6, GW 786034 543726-73-4, IMC 1C11 591207-53-3, LAQ 824 656247-17-5 660412-20-4 660412-24-8 660412-26-0 660412-27-1 660412-28-2 660412-29-3 660412-30-6 660412-31-7 660412-33-9 698387-09-6, HKI 272 790241-27-9 790241-28-0 790241-29-1 790241-30-4 790241-31-5 790713-23-4, MD 275 (pharmaceutical) 790713-30-3, BAY 57-9006 790713-36-9, IM 842 790713-55-2, AZD 6474 790713-57-4, BMY 42355 791073-97-7, 1D09C3 892553-42-3, Vitaxin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug combinations for diseases involving cell proliferation and migration or apoptosis or angiogenesis including protein tyrosine kinase receptor antagonists and radiotherapy)

L110 ANSWER 24 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:817864 HCAPLUS Full-text
DOCUMENT NUMBER: 141:314164
TITLE: preparation of pyridinyloxyphenylethanediamide derivs. as RAF-kinase inhibitors
INVENTOR(S): Buchstaller, Hans-Peter; Wiesner, Matthias; Zenke, Frank; Amendt, Christiane; Grell, Matthias; Sirrenberg, Christian
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 197 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

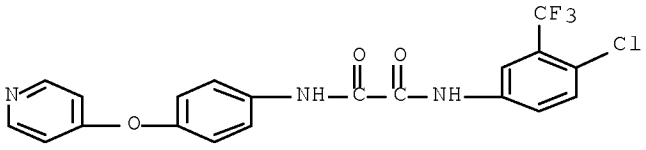
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085399	A1	20041007	WO 2004-EP2406	20040309 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004224239	A1	20041007	AU 2004-224239	20040309 <--
CA 2520009	A1	20041007	CA 2004-2520009	20040309 <--
EP 1606260	A1	20051221	EP 2004-718645	20040309 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004007968	A	20060307	BR 2004-7968	20040309 <--
CN 1764645	A	20060426	CN 2004-80007867	20040309 <--
JP 2006521304	T	20060921	JP 2006-504603	20040309 <--
US 20060189665	A1	20060824	US 2005-549852	20050923 <--
PRIORITY APPLN. INFO.:			EP 2003-6702 A	20030324 <--
			WO 2004-EP2406 W	20040309

OTHER SOURCE(S): CASREACT 141:314164; MARPAT 141:314164

AB ADB [D = (substituted) bivalent oxamide moiety; A = L(ML1)a; L = 5-7 membered cyclic structure, preferably aryl, heteroaryl, arylene, heteroarylene; L1 = (substituted) cyclic moiety having at least 5 members, preferably aryl, heteroaryl, aralkyl, cycloalkyl, heterocyclyl; M = bond, bridging group; a = 1-4; L, L1 contain 0-4 N, O, S atoms; B = (substituted) up to tricyclic aryl, heteroaryl containing 0-4 N, O, S atoms], were prepared for treatment of hyperproliferative and nonhyperproliferative disorders (no data). For example, reaction of N-(4-chloro-3- trifluoromethylphenyl)-2-oxoglycine (preparation given) with 4-(4-pyridinyloxy)phenylamine yielded N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-(4-pyridinyloxy)phenyl]ethanediamine.

IT 767358-34-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridinyloxyphenylethanediamide derivs. as RAF-kinase inhibitors)

RN 767358-34-9 HCAPLUS
CN Ethanediamide, N1-[4-chloro-3-(trifluoromethyl)phenyl]-N2-[4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)



IC ICM C07D213-68

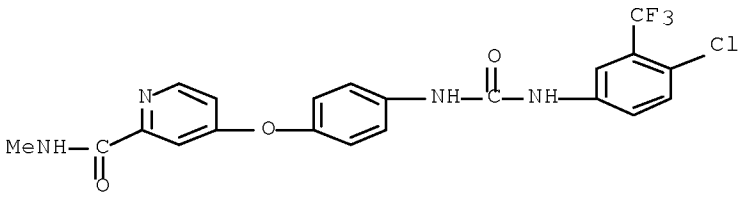
ICS C07D413-12; C07D213-81; A61P031-00; A61K031-4427; A61P017-06
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
IT 767358-34-9P 767358-35-0P 767358-36-1P 767358-37-2P
767358-38-3P 767358-39-4P 767358-40-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridinyloxyphenylethanediamide derivs. as RAF-kinase inhibitors)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 25 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:802884 HCAPLUS Full-text
DOCUMENT NUMBER: 141:289056
TITLE: Medical use of ras antagonists for the treatment of capillary malformation
INVENTOR(S): Vikkula, Miikka; Boon, Laurence; Eerola, Iiro
PATENT ASSIGNEE(S): Universite Catholique De Louvain, Belg.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004083458	A1	20040930	WO 2003-EP2913	20030320 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2515519	A1	20040930	CA 2003-2515519	20030320 <--
AU 2003214145	A1	20041011	AU 2003-214145	20030320 <--
EP 1604037	A1	20051214	EP 2003-709806	20030320 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20060141472	A1	20060629	US 2005-546692	20050928 <--
PRIORITY APPLN. INFO.:			WO 2003-EP2913 W	20030320 <--

AB The invention relates to the field of vascular anomalies and methods for diagnosing and treating them. The invention provides for the causative gene (RASA1) and mutations therein which are useful for diagnosing inherited capillary malformations. The invention further provides RASA1 antagonists for use in treatment of capillary malformations.
IT 284461-73-0, BAY 43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Raf protein inhibitor; diagnosis and treatment of vascular anomalies using primers to detect RASA1 gene mutations and ras protein antagonists)
RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]c

arbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C12Q001-68
ICS A61K031-00
CC 1-8 (Pharmacology)
Section cross-reference(s): 3
IT 177075-18-2, ISIS 5132 284461-73-0, BAY 43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Raf protein inhibitor; diagnosis and treatment of vascular anomalies using primers to detect RASA1 gene mutations and ras protein antagonists)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 26 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:756710 HCAPLUS Full-text
DOCUMENT NUMBER: 141:277628
TITLE: Preparation of ureidophenoxycyanopyridines as anticancer drugs.
INVENTOR(S): Scott, William J.; Dumas, Jacques; Boyer, Stephen; Lee, Wendy; Chen, Yuanwei; Phillips, Barton; Verma, Sharad; Chen, Jianqing; Chen, Zhi; Fan, Jianmei; Raudenbush, Brian; Redman, Aniko; Yi, Lin; Zhu, Qingming
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078747	A1	20040916	WO 2004-US6286	20040301 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20040235829	A1	20041125	US 2004-788029	20040227 <--
AU 2004217977	A1	20040916	AU 2004-217977	20040301 <--
CA 2517361	A1	20040916	CA 2004-2517361	20040301 <--

US 20040229937	A1	20041118	US 2004-789446		20040301 <--
US 20050032798	A1	20050210	US 2004-788405		20040301 <--
US 20050038031	A1	20050217	US 2004-788426		20040301 <--
EP 1599467	A1	20051130	EP 2004-716144		20040301 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK					
BR 2004007897	A	20060301	BR 2004-7897		20040301 <--
JP 2006519264	T	20060824	JP 2006-508977		20040301 <--
CN 1839126	A	20060927	CN 2004-80011547		20040301 <--
IN 2005DN03802	A	20070824	IN 2005-DN3802		20050826 <--
PRIORITY APPLN. INFO.:			US 2003-450323P	P	20030228 <--
			US 2003-450324P	P	20030228 <--
			US 2003-450348P	P	20030228 <--
			WO 2004-US6286	A	20040301

OTHER SOURCE(S): CASREACT 141:277628; MARPAT 141:277628

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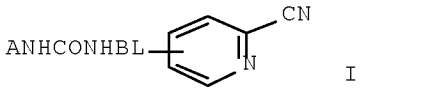

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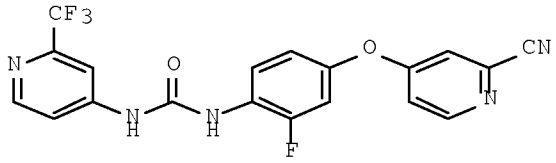


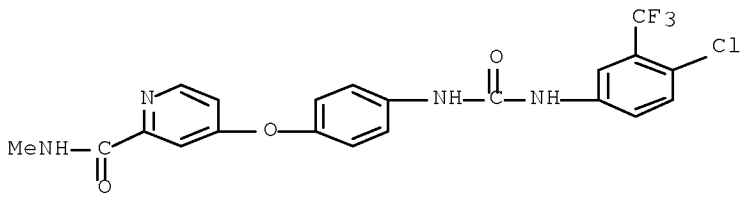
II

AB Title compds. [I; A = (substituted) pyridinyl, naphthyl, 8-10 membered bicyclic heteroaryl, heterocyclyl, carbocyclyl; B = (substituted) phenylene, naphthylenediyl; L = O, S; m = 0-3; R2 = alkyl, haloalkyl, alkoxy, N-oxo, N-hydroxy], were prepared Thus, 2-trifluoromethyl-4- pyridylamine was stirred 20 h with carbonyldiimidazole in CH2Cl2; 4-(4-amino-3-fluorophenoxy)pyridine-2-carbonitrile (preparation given) was added followed by stirring for 1 day to give 75% title compound (II). I inhibited c-RAF-1 kinase with IC50 = 7.86 nM to >1600 nM.

IT 284461-73-0, Bay 43-9006
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of ureidophenoxycyanopyridines as anticancer drugs)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)

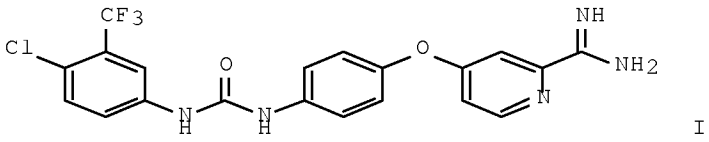


IC ICM C07D401-12
ICS C07D405-12; C07D213-79; C07D417-12; A61K031-443; A61K031-444; A61K031-4433; A61K031-4436; A61P035-00
CC 28-11 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 27, 63
IT 184475-35-2, Iressa 190977-41-4, Oblimersen 191732-72-6, CDC 501 192185-72-1, Tipifarnib 193275-84-2, Lonafarnib 195533-53-0, T-138067 196488-72-9, Ranpirnase 198153-51-4, Pegasys 199396-76-4, Asoprisnil 199796-52-6, Taxoprexin 205923-56-4, Cetuximab 206181-63-7, Ibritumomab tiuxetan 208265-92-3, Neulasta 208921-02-2, Tositumomab 209810-58-2, Aranesp 212141-54-3, Vatalanib 215647-85-1, PEG-intron 216503-57-0, Campath 216586-46-8, Virulizin 216974-75-3, Avastin 219989-84-1, Ixabepilone 220127-57-1, Gleevec 220578-59-6, Gemtuzumab ozogamicin 220581-49-7, Rebif 223378-40-3, Alferon N 263351-82-2, CT-2103 284461-73-0, Bay 43-9006 305838-77-1, Neovastat 416841-63-9, Alfaferone 439943-59-6, Tlk-286 606967-38-8, MX 6 646032-04-4, R 1549 675625-06-6, Affinitak
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of ureidophenoxycyanopyridines as anticancer drugs)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 27 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:754414 HCAPLUS Full-text
DOCUMENT NUMBER: 141:277492
TITLE: Preparation of pyridine-containing diaryl ureas useful in the treatment of cancer and other disorders
INVENTOR(S): Dumas, Jacques; Lee, Wendy; Chen, Yuanwei; Adnane, Lila; Scott, William J.; Verma, Sharad; Chen, Jianging; Chen, Zhi; Yi, Lin
PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004078128	A2	20040916	WO 2004-US6295		20040301 <--
WO 2004078128	A3	20041223			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2516627	A1	20040916	CA 2004-2516627		20040301 <--
EP 1603879	A2	20051214	EP 2004-716142		20040301 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK					
JP 2006519266	T	20060824	JP 2006-508981		20040301 <--
MX 2005PA09102	A	20060531	MX 2005-PA9102		20050826 <--
PRIORITY APPLN. INFO.:			US 2003-450324P	P	20030228 <--
			WO 2004-US6295	W	20040301

OTHER SOURCE(S): MARPAT 141:277492
GI

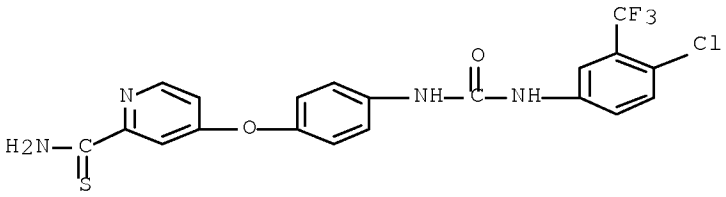


I

AB The title novel pyridine-containing diaryl ureas ANHC(O)NHBLMQ [A = (un)substituted Ph, naphthyl, heteroaryl, etc.; B = (un)substituted Ph, naphthyl, pyridyl; L = (CH2)mO(CH2)l, (CH2)m(CH2)l, (CH2)mC(O)(CH2)l, etc.; m, l = 0-4; M = (un)substituted pyridine; Q = tetrazolyl, imidazolyl, thiazolinyl, etc.], useful for treating hyper-proliferative and angiogenesis disorders, as a sole agent or in combination with cytotoxic therapies, were prepared and formulated. E.g., a multi-step synthesis of I, was given.

IT 758709-43-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyridine-containing diaryl ureas for treating cancer and other disorders)

RN 758709-43-2 HCAPLUS
CN 2-Pyridinecarbothioamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM A61K
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

IT 758709-43-2P 758709-45-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyridine-containing diaryl ureas for treating cancer and other disorders)

IT 758709-37-4P 758709-38-5P 758709-40-9P 758709-41-0P
758709-47-6P 758709-49-8P 758709-51-2P 758709-53-4P
758709-55-6P 758709-57-8P 758709-59-0P 758709-61-4P
758709-63-6P 758709-65-8P 758709-67-0P
758709-69-2P 758709-71-6P 758709-73-8P

758709-75-0P 758709-77-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridine-containing diaryl ureas for treating cancer and other disorders)
IT 24484-93-3P 51727-15-2P 73771-11-6P 220000-87-3P
228400-44-0P 284462-37-9P 284462-78-8P 573673-43-5P
630125-69-8P 757229-80-4P 757230-16-3P 757249-68-6P 757250-67-2P
757251-59-5P 757251-60-8P 757251-79-9P 758709-84-1P 758709-88-5P
758709-89-6P 758709-90-9P 758709-91-0P 758709-92-1P
758709-93-2P 758709-94-3P 758709-95-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyridine-containing diaryl ureas for treating cancer and other disorders)

L110 ANSWER 28 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:428911 HCAPLUS Full-text
DOCUMENT NUMBER: 141:7028
TITLE: Preparation of 3-substituted-6-aryl pyridines ligands of C5a receptors
INVENTOR(S): Hutchison, Alan; Yuan, Jun; Lee, Kyungae; Maynard, George; Chenard, Bertrand L.; Liu, Nian; Guo, Qin; Guo, Zihong; Hrnciar, Peter
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 366 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043925	A2	20040527	WO 2003-US35694	20031107 <--
WO 2004043925	A3	20040805		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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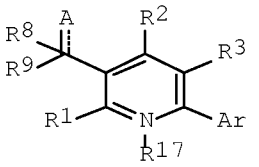
AU 2003291403	A1	20040603	AU 2003-291403	20031107 <--
US 20040158067	A1	20040812	US 2003-704364	20031107 <--
US 7342115	B2	20080311		
EP 1565452	A2	20050824	EP 2003-768799	20031107 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-425281P P 20021108 <--
WO 2003-US35694 W 20031107 <--
OTHER SOURCE(S): MARPAT 141:7028
GI



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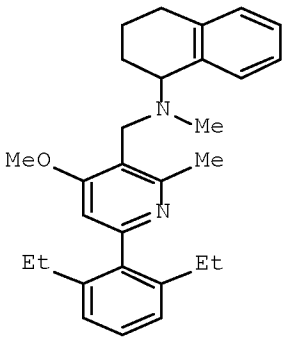


II

AB The title compds. [I; Ar = (un)substituted Ph, naphthyl, pyridyl, etc.; A = OR4, NR4R5, CR6R7, CHR6R7; R1 = H, halo, NH2, CN, etc.; R2 = halo, CN, XR; R3 = H, halo, OH, etc.; R4 = alkyl, alkenyl, benzoisothiazolyl, etc.; R5 = H, alkyl, alkenyl, etc.; R6 = halo, OH, CN, etc.; R7 = H, halo, OH, etc.; R8 = H, halo, OH, etc.; R9 = absent, H, halo, OH, etc.; X = a bond, O, CO, etc.; R = H, alkyl, alkenyl, etc.; R17 = absent, O] which bind to C5a receptors with high affinity and exhibit neutral antagonist or inverse agonist activity at C5a receptors, and therefore are useful in treating a variety of inflammatory, cardiovascular, and immune system disorders, were prepared and formulated. E.g., a multi-step synthesis of II is given. In addition, the present invention provides labeled 3-substituted-6-aryl pyridines I, which are useful as probes for the localization of C5a receptors.

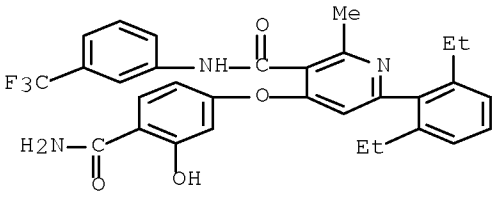
IT 693277-81-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 3-substituted-6-aryl pyridines as ligands of C5a receptors)

RN 693277-81-5 HCAPLUS

CN 3-Pyridinecarboxamide, 4-[4-(aminocarbonyl)-3-hydroxyphenoxy]-6-(2,6-diethylphenyl)-2-methyl-N-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



IC ICM C07D213-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 63

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693276-93-6P 693276-94-7P 693276-95-8P 693276-96-9P 693276-97-0P
693276-98-1P 693276-99-2P 693277-00-8P 693277-01-9P 693277-02-0P

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693279-25-3P 693279-26-4P 693279-27-5P 693279-28-6P 693279-29-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-substituted-6-aryl pyridines as ligands of C5a receptors)

L110 ANSWER 29 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:370904 HCAPLUS Full-text
DOCUMENT NUMBER: 140:391200
TITLE: Preparation of pyridinyloxybenzylureas as RAF kinase inhibitors.
INVENTOR(S): Buchstaller, Hans-Peter; Wiesner, Matthias; Schadt, Oliver; Amendt, Christiane; Zenke, Frank; Sirrenberg, Christian; Grell, Matthias; Finsinger, Dirk
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 341 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037789	A2	20040506	WO 2003-EP11134	20031008 <--
WO 2004037789	A3	20041028		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2503445	A1	20040506	CA 2003-2503445	20031008 <--
AU 2003268926	A1	20040513	AU 2003-268926	20031008 <--
EP 1562905	A2	20050817	EP 2003-750697	20031008 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015580	A	20050830	BR 2003-15580	20031008 <--
CN 1705645	A	20051207	CN 2003-80101925	20031008 <--
JP 2006506454	T	20060223	JP 2005-501513	20031008 <--
MX 2005PA04206	A	20050608	MX 2005-PA4206	20050420 <--
US 20060199844	A1	20060907	US 2005-532574	20050425 <--
ZA 2005004175	A	20060329	ZA 2005-4175	20060117 <--
PRIORITY APPLN. INFO.:			EP 2002-23906 A	20021024 <--
			US 2003-490285P P	20030728 <--
			WO 2003-EP11134 W	20031008 <--

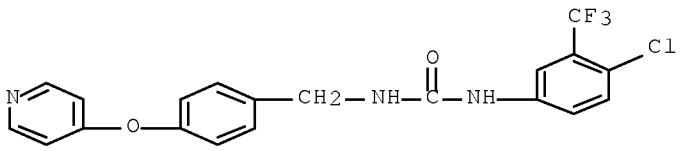
OTHER SOURCE(S): MARPAT 140:391200

AB ADB [D = methyleneurea moiety or derivative thereof; A = (substituted) L(ML')a; L = 5-7 membered cyclic structure, e.g. aryl, heteroaryl, arylene, heteroarylene; L' = (substituted) cyclic moiety having ≥5 members, e.g. aryl, heteroaryl, aralkyl, cycloalkyl, heterocyclyl; M = bond, bridging group having ≥1 atom; a = 1-4; B = (substituted) up to tricyclic aryl, heteroaryl], were prepared for treatment of hyperproliferative and nonproliferative disorders (no data). Thus, 4-(4-pyridinyloxy)benzylamine (preparation given) and 4-chloro-3- trifluoromethylphenyl isocyanate were stirred together for 2 h in CH2Cl2 to give 1-(4-chloro-3-trifluoromethylphenyl)-3-[4-(4-pyridinyloxy)benzyl]urea.

IT 685533-65-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of methylene urea derivs. as RAF kinase inhibitors)

RN 685533-65-7 HCAPLUS

CN Urea, N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[[4-(4-pyridinyloxy)phenyl]methyl]- (CA INDEX NAME)



IC ICM C07D213-00
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
IT 685533-65-7P 685533-66-8P 685533-67-9P 685533-68-0P
685533-69-1P 685533-70-4P 685533-71-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of methylene urea derivs. as RAF kinase inhibitors)
IT 74-89-5, Methylamine, reactions 76-02-8, Trichloroacetyl chloride 98-98-6, Pyridine-2-carboxylic acid 99-93-4, 4-Hydroxyacetophenone 108-01-0, 2-Dimethylaminoethanol 109-00-2, 3-Hydroxypyridine 327-78-6, 4-Chloro-3-trifluoromethylphenyl isocyanate 367-86-2, 4-Fluoro-3-nitrobenzotrifluoride 619-24-9, 3-Nitrobenzonitrile 626-55-1, 3-Bromopyridine 767-00-0, 4-Hydroxybenzonitrile 873-62-1, 3-Hydroxybenzonitrile 6627-53-8, 5-Chloro-2-nitroanisole 55809-36-4, 3-Amino-5-tert-butylisoxazole 56201-88-8 685534-00-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of methylene urea derivs. as RAF kinase inhibitors)

L110 ANSWER 30 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:203667 HCAPLUS Full-text
DOCUMENT NUMBER: 140:253554
TITLE: Preparation of pyridinyloxyphenylaminoacetamides as RAF kinase inhibitors
INVENTOR(S): Buchstaller, Hans-Peter; Wiesner, Matthias; Schadt, Oliver; Amendt, Christiane; Zenke, Frank; Sirrenberg, Christian; Grell, Matthias
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 182 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004019941	A1	20040311	WO 2003-EP8474	20030731 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2496688	A1	20040311	CA 2003-2496688	20030731 <--
AU 2003250197	A1	20040319	AU 2003-250197	20030731 <--

EP 1531817 A1 20050525 EP 2003-790841 20030731 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
CN 1678314 A 20051005 CN 2003-820571 20030731 <--
JP 2005539041 T 20051222 JP 2004-531844 20030731 <--
US 20060167261 A1 20060727 US 2005-526043 20050228 <--
PRIORITY APPLN. INFO.: EP 2002-19023 A 20020827 <--
WO 2003-EP8474 W 20030731 <--

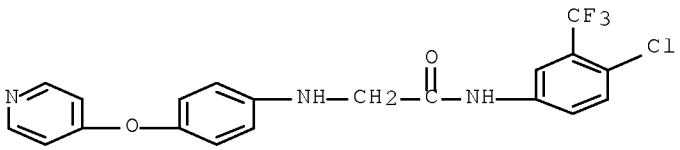
OTHER SOURCE(S): MARPAT 140:253554

AB ADB [D = (substituted) bivalent glycinamide moiety; A = L(ML1)a; L = 5-7 membered cyclic structure, preferably aryl, heteroaryl, arylene, heteroarylene; L1 = (substituted) cyclic moiety having ≥5 members, preferably aryl, heteroaryl, aralkyl, cycloalkyl, heterocyclyl; M = bond, bridging group; a = 1-4; L, L1 contain 0-4 N, O, S atoms; B = (substituted) up to tricyclic aryl, heteroaryl containing 0-4 N, O, S atoms], were prepared for treatment of hyperproliferative and nonhyperproliferative disorders (no data). Thus, 3-(4-pyridinyloxy)aniline (preparation given), N-(5-tert-butyl-3-isoxazolyl)-2-chloroacetamide (preparation given), and diisopropylethylamine were heated in DMF at 100° for 4 h to give 48% N-(5-tert-butyl-3-isoxazolyl)-2-[3-(4-pyridinyloxy)phenylamino]acetami de.

IT 668980-73-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridinyloxyphenylaminoacetamides as RAF kinase inhibitors)

RN 668980-73-2 HCAPLUS

CN Acetamide, N-[4-chloro-3-(trifluoromethyl)phenyl]-2-[[4-(4-pyridinyloxy)phenyl]amino]- (CA INDEX NAME)



IC ICM A61K031-4409
ICS A61K031-4427; C07D213-68; C07D413-12; A61P035-00

CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 27

IT 668980-73-2P 668980-74-3P 668980-75-4P 668980-76-5P 668980-77-6P 668980-78-7P 668980-79-8P 668980-80-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridinyloxyphenylaminoacetamides as RAF kinase inhibitors)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 31 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:533967 HCAPLUS Full-text
DOCUMENT NUMBER: 141:65147
TITLE: Method for treating diseases associated with abnormal tyrosine kinase activity by administering a DNA methylation inhibitor and a tyrosine kinase inhibitor
INVENTOR(S): Lyons, John; Rubinfeld, Joseph

PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of U.S. Ser. No. 71,849.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040127453	A1	20040701	US 2002-206854	20020726 <--
US 6998391	B2	20060214		
US 20030147813	A1	20030807	US 2002-71849	20020207 <--
CA 2474174	A1	20030814	CA 2003-2474174	20030206 <--
WO 2003065995	A2	20030814	WO 2003-US3537	20030206 <--
WO 2003065995	A3	20051013		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003215065	A1	20030902	AU 2003-215065	20030206 <--
EP 1572075	A2	20050914	EP 2003-710881	20030206 <--
EP 1572075	A3	20051207		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20060140947	A1	20060629	US 2005-181368	20050713 <--

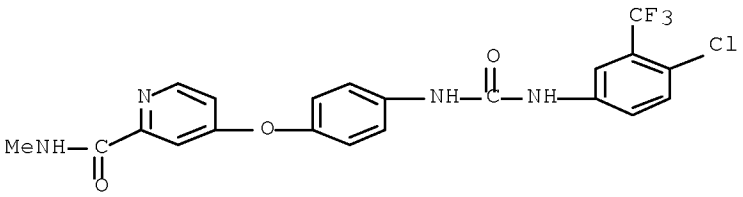
PRIORITY APPLN. INFO.:
US 2002-71849 A2 20020207 <--
US 2002-206854 A 20020726 <--
WO 2003-US3537 W 20030206 <--

AB Methods are provided for treating diseases associated with abnormal activity of kinases. The method comprises: administering a DNA methylation inhibitor to the patient in therapeutically effective amount; and administering a kinase inhibitor to the patient in therapeutically effective amount, such that the in vivo activity of the kinase is reduced relative to that prior to the treatment. The method can be used to treat cancer associated with abnormal activity of kinases such as phosphatidylinositol 3'-kinase (PI3K), protein kinases including serine/threonine kinases such as Raf kinases, protein kinase kinases such as MEK, and tyrosine kinases such as those in the epidermal growth factor receptor family (EGFR), platelet-derived growth factor receptor family (PDGFR), vascular endothelial growth factor receptor (VEGFR) family, nerve growth factor receptor family (NGFR), fibroblast growth factor receptor family (FGFR) insulin receptor family, ephrin receptor family, Met family, Ror family, c-kit family, Src family, Fes family, JAK family, Fak family, Btk family, Syk/ZAP-70 family, and Abl family.

IT 284461-73-0, BAY 43-9006
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Raf kinase inhibitor; treating diseases associated with abnormal tyrosine kinase activity by administering DNA methylation inhibitors and tyrosine kinase inhibitors)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-7072
INCL 514050000
CC 1-12 (Pharmacology)
Section cross-reference(s): 7
IT 284461-73-0, BAY 43-9006
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Raf kinase inhibitor; treating diseases associated with abnormal tyrosine kinase activity by administering DNA methylation inhibitors and tyrosine kinase inhibitors)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 32 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:513393 HCAPLUS Full-text
DOCUMENT NUMBER: 141:71544
TITLE: Preparation of substituted benzazoles as Raf kinase inhibitors
INVENTOR(S): Amiri, Payman; Fantl, Wendy; Levine, Barry Haskell; Poon, Daniel J.; Ramurthy, Savithri; Renhowe, Paul A.; Subramanian, Sharadha; Sung, Leonard
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 476 pp., Cont.-in-part of U.S. Pat. Appl. 2004 87,626.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040122237	A1	20040624	US 2003-675927	20030929 <--
US 20040087626	A1	20040506	US 2003-405945	20030331 <--
US 7071216	B2	20060704		
AU 2004277405	A1	20050414	AU 2004-277405	20040929 <--
CA 2539748	A1	20050414	CA 2004-2539748	20040929 <--
WO 2005032548	A1	20050414	WO 2004-US32161	20040929 <--

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

EP 1675584	A1	20060705	EP 2004-789345		20040929	<--
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BR 2004014908	A	20061107	BR 2004-14908		20040929	<--
CN 1913884	A	20070214	CN 2004-80032677		20040929	<--
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US 20070299039	A1	20071227	US 2005-282939		20051118	<--
MX 2006PA03435	A	20060620	MX 2006-PA3435		20060327	<--
JP 2006193533	A	20060727	JP 2006-96143		20060330	<--
IN 2006KN00838	A	20070413	IN 2006-KN838		20060405	<--
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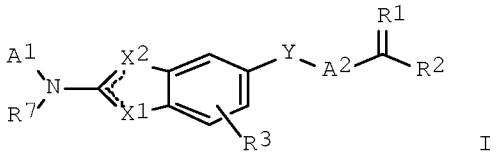
			US 2003-405945	A2	20030331	<--
			JP 2003-579810	A3	20030331	<--
			US 2003-675927	A	20030929	<--
			WO 2004-US32161	W	20040929	

OTHER SOURCE(S): MARPAT 141:71544

GI



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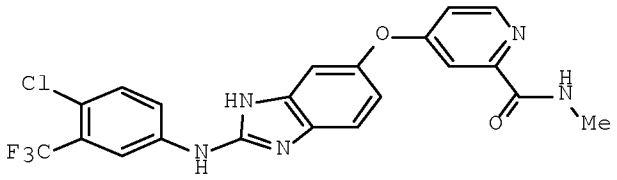


II

AB The title compds. I [wherein X1, X2 = N, NR4, O, S (with provisos); Y = O, S; A1 = (un)substituted alkyl, (hetero)cycloalkyl(alkyl), (hetero)aryl(alkyl), etc.; A2 = (un)substituted heteroaryl; R1 = O, H; R2 = NR5R6, OH; or CR1R2 = (un)substituted heterocycloalkyl, heteroaryl; R3 = H, halo, alkyl, alkoxy; R4 = H, OH, (di)alkylamino, alkyl; R5, R6 = H, (un)substituted (cyclo)alkyl, alkoxyalkyl, aminoalkyl, amidoalkyl, acyl, heterocyclyl, (hetero)aryl, etc.; or R5 and R6 are taken together to form (un)substituted heterocyclyl or heteroaryl; R7 = alkyl; and pharmaceutically acceptable salts, esters, or prodrugs] were prepared as Raf kinase inhibitors. Examples include synthetic methods and phys. data for 1400 compds., as well as descriptions of two Raf kinase bioassays. For instance, 4-amino-3-nitrophenol and (4-chloropyridin-2-yl)-N- methylcarboxamide were coupled using potassium bis(trimethylsilyl)amide and K2CO3 in DMF to give 4-[(4-amino-3-nitrophenyl)oxy]-N-methylpyridine-2-carboxamide. Pd-catalyzed hydrogenation, followed by cyclization with 4-chloro-3-(trifluoromethyl)benzeneisothiocyanate in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide•HCl in THF provided the benzimidazole II. One thousand ninety-four compds. inhibited Raf kinase activity with IC50 < 5 μM in a Raf/Mek filtration assay or a biotinylated Raf screen. Thus, I and

their pharmaceutical compns., which may comprise at least one addnl. agent, are useful for the treatment of Raf kinase mediated disorders, such as cancer (no data).

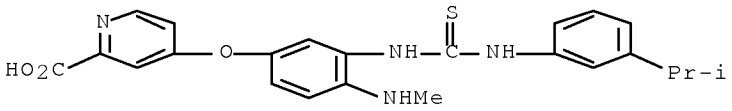
IT 611225-97-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of substituted benzazoles as Raf kinase inhibitors for treatment of cancer)

RN 611225-97-9 HCAPLUS

CN 2-Pyridinecarboxylic acid, 4-[4-(methylamino)-3-[[[[3-(1-methylethyl)phenyl]amino]thioxomethyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM C07D277-82

ICS C07D263-60

INCL 548161000; 548217000

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

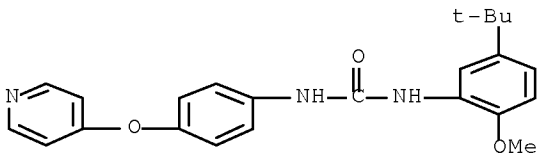
IT 656-64-4P 823-54-1P 3530-00-5P, 3-Phenoxyphenylisothiocyanate 6358-77-6P 7748-59-6P 7748-60-9P 20734-76-3P 23491-48-7P 49559-34-4P 49559-83-3P 54998-08-2P 79110-05-7P 106146-35-4P 114780-06-2P 115619-00-6P 115619-01-7P 120381-42-2P 127142-66-9P, (4-Chloro-3-nitrophenyl)isothiocyanate 129488-00-2P 191602-42-3P 191602-43-4P, (3-Bromo-4-isopropoxyphenyl)amine 210158-20-6P 211635-75-5P 214337-39-0P 219552-64-4P 220000-86-2P 239122-51-1P 262368-47-8P 284462-57-3P 284462-58-4P 401815-98-3P 402948-23-6P 402948-25-8P 402948-26-9P 414880-35-6P 483324-01-2P 485841-45-0P 485841-46-1P 485841-47-2P 485841-49-4P 597545-16-9P 611225-42-4P 611225-43-5P 611225-44-6P 611225-45-7P 611225-46-8P 611225-52-6P 611225-53-7P 611225-54-8P 611225-58-2P 611225-59-3P 611225-60-6P 611225-61-7P 611225-62-8P 611225-63-9P 611225-64-0P 611225-65-1P 611225-66-2P 611225-67-3P 611225-68-4P 611225-69-5P 611225-70-8P 611225-71-9P 611225-72-0P 611225-73-1P 611225-74-2P 611225-75-3P 611225-76-4P 611225-77-5P 611225-78-6P 611225-79-7P 611225-80-0P 611225-81-1P 611225-82-2P 611225-83-3P 611225-84-4P 611225-85-5P 611225-86-6P 611225-87-7P 611225-88-8P 611225-89-9P 611225-90-2P 611225-91-3P 611225-92-4P 611225-93-5P 611225-94-6P 611225-95-7P 611225-96-8P 611225-97-9P 611225-98-0P 611225-99-1P 611226-00-7P 611226-01-8P 611226-02-9P 611226-03-0P 611226-04-1P 611226-05-2P 611226-06-3P 611226-07-4P 611226-08-5P 611226-09-6P 611226-11-0P 611226-12-1P 611226-13-2P 611226-14-3P 611226-15-4P 611226-17-6P 611226-18-7P 611226-19-8P 611226-20-1P 611226-21-2P 611226-22-3P 611226-23-4P 611226-24-5P 611226-25-6P 611226-26-7P 611226-27-8P 611226-28-9P 611226-29-0P 611226-30-3P 611226-31-4P 611226-32-5P 611226-33-6P 611226-34-7P 710351-24-9P 710351-27-2P 710351-29-4P 710351-30-7P 710351-32-9P 710351-65-8P 710351-66-9P 710351-70-5P, 1-(2-Methyl-5-nitrophenyl)pyrrolidine 710351-71-6P, [4-Methyl-3-(pyrrolidin-1-yl)phenyl]amine 710351-72-7P, [4-Methyl-3-(pyrrolidin-1-yl)phenyl]isothiocyanate 710351-74-9P, 4-[[2-[(4-Chloro-3-nitrophenyl)amino]-1-methylbenzimidazol-5-yl]oxy]-N-methylpyridine-2-carboxamide 710351-75-0P, 4-[[2-[(3-Amino-4-chlorophenyl)amino]-1-methylbenzimidazol-5-yl]oxy]-N-methylpyridine-2-

carboxamide 710351-78-3P, 4-[4-(Methylamino)-3-nitrophenoxy]pyridine-2-carboxamide 710351-79-4P, 4-[3-Amino-4-(methylamino)phenoxy]pyridine-2-carboxamide 710351-81-8P, 1-[2-(3-Nitrophenyl)ethyl]pyrrolidine 710351-82-9P, [3-[2-(Pyrrolidin-1-yl)ethyl]phenyl]amine 710351-83-0P, [3-[2-(Pyrrolidin-1-yl)ethyl]phenyl]isothiocyanate 710351-84-1P, [3-Bromo-4-(2,2,2-trifluoroethoxy)phenyl]amine 710351-85-2P, 2-Bromo-4-nitro-1-(2,2,2-trifluoroethoxy)benzene 710351-86-3P, 3-Isopropyl-4-fluoroaniline 710351-87-4P, 4-Methyl-3-(3-furyl)nitrobenzene 710351-88-5P, 4-Methyl-3-(3-furyl)aniline 710351-89-6P, 4-Methyl-3-(tetrahydrofuran-3-yl)aniline
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of substituted benzazoles as Raf kinase inhibitors for treatment of cancer)

L110 ANSWER 33 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:433797 HCAPLUS Full-text
DOCUMENT NUMBER: 140:423477
TITLE: Preparation of diaryl ureas as inhibitors of p38 kinase
INVENTOR(S): Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David E.; Hatoum-Mokdad, Holia; Rodriguez, Marell; Sibley, Robert; Wang, Ming; Turner, Tiffany; Brennan, Catherine
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 60 pp., Cont. of U.S. Ser. No. 458,015, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20040102636	A1	20040527	US 2002-60396		20020201 <--
PRIORITY APPLN. INFO.:			US 1997-126439P	P	19971222 <--
			US 1998-285522	B1	19981222 <--
			US 1999-458015	B1	19991210 <--

OTHER SOURCE(S): MARPAT 140:423477
AB A method of treating a p-38 mediated disease other than cancer comprises administration of BNHCONHA [A = (substituted) Ph, pyridyl, 2-thienyl; B = (substituted) aryl, heteroaryl containing ≥1 6-membered aromatic structure containing 0-4 N, O, or S atoms]. Thus, 5-tert-butyl-2-(3-tetrahydrofuranyloxy)aniline (preparation given) and p-tolyl isocyanate were stirred 8 h in PhMe to give 75% N-(5-tert-butyl-2-(3-tetrahydrofuranyloxy)phenyl)-N'-(4-methylphenyl)urea. Title compds. inhibited p38 kinase with IC50 = 1-10 μM.
IT 228399-41-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diaryl ureas as inhibitors of p38 kinase)
RN 228399-41-5 HCAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)



IC ICM A61K031-44
ICS A61K031-381; A61K031-325; A61K031-277; A61K031-17; A61K031-216; A61K031-195
INCL 546306000; 549069000; 558418000; 560024000; 564050000; 564049000; 514349000; 514447000; 514485000; 514522000
CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 27, 28, 63
IT 370-50-3P 117745-34-3P 228399-32-4P 228399-33-5P 228399-34-6P
228399-35-7P 228399-38-0P 228399-41-5P 228399-44-8P
228399-45-9P 228399-61-9P 228399-62-0P 228399-63-1P 228399-65-3P
228399-66-4P 228399-68-6P 228399-69-7P 228399-70-0P 228399-71-1P
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228418-42-6P 228418-48-2P 228418-49-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diaryl ureas as inhibitors of p38 kinase)

L110 ANSWER 34 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:182368 HCAPLUS Full-text
DOCUMENT NUMBER: 140:229401
TITLE: Three hybrid assay system for isolating ligand-binding

polypeptides and for isolating small mol. ligands
INVENTOR(S): Come, Jon H.; Becker, Frank; Kley, Nikolai A.; Reichel, Christoph
PATENT ASSIGNEE(S): Gpc Biotech Inc., USA; Gpc Biotech AG
SOURCE: U.S. Pat. Appl. Publ., 238 pp., Cont.-in-part of U.S. Ser. No. 91,177.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040043388	A1	20040304	US 2002-234985	20020903 <--
US 7135550	B2	20061114		
US 20030165873	A1	20030904	US 2002-91177	20020304 <--
EP 1832589	A1	20070912	EP 2007-8359	20021015 <--
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, SK, TR, AL, LT, LV, MK				
US 20040266854	A1	20041230	US 2004-820453	20040407 <--

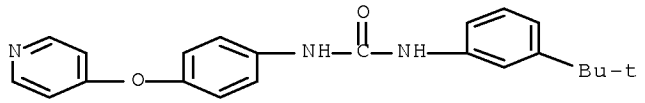
PRIORITY APPLN. INFO.:

US 2001-272932P	P	20010302 <--
US 2001-278233P	P	20010323 <--
US 2001-329437P	P	20011015 <--
US 2002-91177	A2	20020304 <--
US 2001-336962P	P	20011203 <--
WO 2002-US6677	A2	20020304 <--
US 2002-234985	A2	20020903 <--
EP 2002-797047	A3	20021015 <--
WO 2002-US33052	A2	20021015 <--
US 2003-460921P	P	20030407 <--
US 2003-531872P	P	20031223 <--

AB The invention provides compns. and methods for isolating ligand-binding polypeptides for a user-specified ligand, and for isolating small mol. ligands for a user-specified target polypeptide using an improved class of hybrid ligand compds. Preparation of compds., e.g a methotrexate moiety linked by a polyethylene gycol moiety to dexamethasone, is described.

IT 228399-50-6D, conjugates
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(three hybrid assay system for isolating ligand-binding polypeptides and for isolating small mol. ligands)

RN 228399-50-6 HCAPLUS
CN Urea, N-[3-(1,1-dimethylethyl)phenyl]-N'-[4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)



IC ICM C12Q001-68
ICS G01N033-53; C07H021-04
INCL 435006000; X43-5 .71; X53-6 2.31; X53-035.0; X55-265.3; X55-250.0; X53-612.3; X54-6 .1; X54-020.0; X53-031.7
CC 1-1 (Pharmacology)

Section cross-reference(s): 9, 28

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RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(three hybrid assay system for isolating ligand-binding polypeptides and for isolating small mol. ligands)

L110 ANSWER 35 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:950982 HCAPLUS Full-text
DOCUMENT NUMBER: 140:16736
TITLE: Preparation of diarylurea derivatives useful for the treatment of protein kinase dependent diseases
INVENTOR(S): Floersheimer, Andreas; Furet, Pascal; Manley, Paul William; Bold, Guido; Boss, Eugen; Guagnano, Vito; Vaupel, Andrea
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099771	A2	20031204	WO 2003-EP5634	20030528 <--

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PRIORITY APPLN. INFO.:				GB 2002-12413 A	20020529 <--
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				WO 2003-EP5634 W	20030528 <--

OTHER SOURCE(S): MARPAT 140:16736

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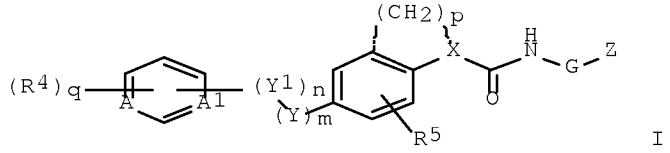


I

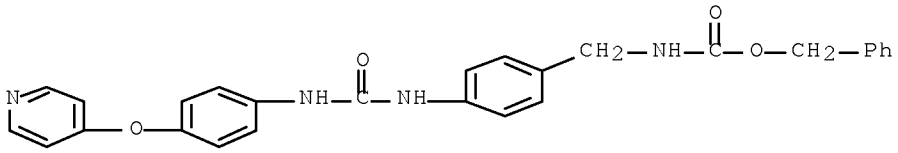
AB The invention relates to the use of diaryl urea derivs. [I; G is not present and Z = a radical of the formula Q; A = CH, N, N→O; A1 = N, N→O, with the proviso that not more than one of A and A1 can be N→O; n = 1, 2; m = 0-2; p = 0, 2, 3; q = 0-5; X = (un)substituted NH if p = 0; or if p is 2 or 3, X = nitrogen which together with (CH2)p and the bonds represented in dotted (interrupted) lines (including the atoms to which they are bound) forms a ring, or X = CHK (wherein K = H or lower alkyl) and p = 0, with the proviso that the bonds represented in dotted lines, if p = 0, are absent; Y1 = O, S, CH2; Y2 = O, S, NH; with the proviso that (Y1)n-(Y2)m does not include O-O, S-S, NH-O, NH-S or S-O groups; R1, R2, R3, R5 = independently H or an inorg. or organic moiety or any two of them together form a lower alkylenedioxy bridge bound via the oxygen atoms, and the remaining one of these moieties is hydrogen or an inorg. or organic moiety; R4 (if present, i.e., if q is not zero) is an inorg. or organic moiety] or tautomers thereof or pharmaceutically acceptable salts thereof in the treatment of protein kinase dependent diseases or for the manufacture of pharmaceutical compns. for use in the treatment of said diseases, especially a proliferative disease depending on any one or more

of the following (tyrosine) protein kinases such as ras, Abl, VEGF-receptor tyrosine kinase, Flt3, and/or Bcr-Abl activity. Also disclosed are the use of the compds. I for the manufacture of pharmaceutical compns. for use in the treatment of said diseases, methods of use of the compds. I in the treatment of said diseases, pharmaceutical prepns. comprising the compds. I for the treatment of said diseases, processes for the manufacture of the compds. I, the use or methods of use of the compds. I as mentioned above, and/or the compds. I for use in the treatment of the animal or human body. For example, N-(4-(pyridin-4-yloxy)phenyl)-N'-(4-2,2,2-trifluoroethoxy-3-trifluoromethylphenyl)urea and N-[4-[6-(4-hydroxyphenylamino)pyrimidin-4-yl]phenyl]-N'-(4-2,2,2-trifluoroethoxy-3-trifluoromethylphenyl)urea at 10 μM inhibited gene c-Abl protein kinase by 98%, Kdr receptor tyrosine kinase by 100 and 96%, resp., and Flt3 receptor tyrosine kinase by 100%.

IT 630125-50-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of diarylurea derivs. useful for the treatment of
protein kinase dependent diseases and proliferative diseases)

RN 630125-50-7 HCAPLUS

CN Carbamic acid, [[4-[[[[4-(4-pyridinyloxy)phenyl]amino]carbonyl]amino]phenyl]methyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



IC ICM C07C275-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 7, 27, 63

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[6-(4-Aminophenoxy)pyrimidin-4-yl](4-methoxyphenyl)amine 630125-44-9P, (4-Methoxyphenyl)[6-(4-nitrophenoxy)pyrimidin-4-yl]amine 630125-45-0P 630125-46-1P 630125-47-2P 630125-48-3P 630125-50-7P 630125-51-8P, [4-(Benzyloxycarbonylaminomethyl)phenyl]carbamic acid tert-butyl ester 630125-52-9P, 4-(4-Ethylpiperazin-1-yl)-3-methoxyphenylamine 630125-53-0P, 1-Ethyl-4-(2-methoxy-4-nitrophenyl)piperazine 630125-54-1P, 3-Methoxy-4-(piperidin-1-ylmethyl)phenylamine 630125-55-2P, 1-(2-Methoxy-4-nitrobenzyl)piperidine 630125-56-3P, (2-Methoxy-4-nitrophenyl)piperidin-1-ylmethanone 630125-57-4P, 4-(4-Ethylaminopyrimidin-6-yloxy)aniline 630125-58-5P, 4-(4-Aminophenoxy)-2-methoxypyridine 630125-59-6P, 2-Methoxy-4-(4-nitrophenoxy)pyridine 630125-60-9P, 1-Methyl-4-(4-nitrophenoxy)-1H-pyridin-2-one 630125-61-0P, 4-(4-Nitrophenoxy)-1H-pyridin-2-one 630125-62-1P, 3-(4-Aminophenoxy)-1H-pyridin-6-one 630125-63-2P, 3-(4-Nitrophenoxy)-1H-pyridin-6-one 630125-64-3P, 4-(6-Methoxypyridin-3-ylmethyl)phenylamine 630125-65-4P 630125-66-5P 630125-67-6P, [4-(4-Aminophenoxy)pyridin-2-yl]pyrrolidin-1-ylmethanone 630125-68-7P 630125-69-8P, 4-(4-Aminophenoxy)pyridine-2-carbonitrile 630125-70-1P, 4-(2-Chloropyridin-4-yloxy)phenylamine 630125-71-2P, 4-(2-Trifluoromethylpyridin-4-yloxy)phenylamine 630125-72-3P, 4-(4-Nitrophenoxy)-2-trifluoromethylpyridine 630125-73-4P, 4-(6-Fluoropyrimidin-4-yloxy)phenylamine 630125-74-5P, 4-(6-Trifluoromethylpyrimidin-4-yloxy)phenylamine 630125-75-6P, [4-(6-Chloropyrimidin-4-ylmethyl)phenyl]carbamic acid tert-butyl ester 630125-76-7P, 4-(6-Chloropyrimidin-4-ylmethyl)phenylamine 630125-77-8P, [4-(6-Hydroxypyrimidin-4-ylmethyl)phenyl]carbamic acid tert-butyl ester 630125-78-9P, [4-(6-Hydroxy-2-mercaptopyrimidin-4-ylmethyl)phenyl]carbamic acid tert-butyl ester 630125-79-0P 630125-80-3P, [6-(4-Aminobenzyl)pyrimidin-4-yl]methylamine 630125-81-4P, 4-[2-(1H-Tetrazol-5-yl)pyridin-4-yloxy]phenylamine 630125-82-5P, 3-Trifluoromethyl-4-(piperidin-1-ylmethyl)phenylamine 630125-83-6P, 2,2,2-Trifluoro-N-(4-piperidin-1-ylmethyl-3-trifluoromethylphenyl)acetamide 630125-84-7P 630125-85-8P 630125-86-9P, 3-Methoxy-4-(4-methylpiperazin-1-ylmethyl)phenylamine 630125-87-0P, 3-Methoxy-4-(4-methylpiperazin-1-ylmethyl)nitrobenzene 630125-88-1P, (4-Methylpiperazin-1-yl)(4-nitro-2-methoxyphenyl)methanone 630125-89-2P, 3-Trifluoromethyl-5-(piperidin-1-ylmethyl)phenylamine 630125-90-5P 630125-91-6P, 3-Trifluoromethyl-4-(4-ethylpiperazin-1-ylmethyl)phenylamine 630125-92-7P 630125-93-8P, 3-(4-Ethylpiperazin-1-ylmethyl)-5-trifluoromethylphenylamine 630125-94-9P, (3-Amino-5-trifluoromethylphenyl)(4-ethylpiperazin-1-yl)methanone 630125-95-0P, (3-Nitro-5-trifluoromethylphenyl)(4-ethylpiperazin-1-yl)methanone 630125-96-1P, 4-Chloro-6-(4-isocyanatophenoxy)pyrimidine 630125-97-2P 630125-98-3P, 3-Amino-N,N-dimethyl-5-trifluoromethylbenzamide 630125-99-4P, [6-(4-Aminophenoxy)pyrimidin-4-yl]methylamine 630126-00-0P, 3-Pyridin-2-yl-5-trifluoromethylphenylamine 630126-01-1P, Methyl[4-(4-nitrophenoxy)pyrimidin-2-yl]amine 630126-02-2P, 2-Chloro-4-(4-nitrophenoxy)pyrimidine 630126-03-3P, 4-(2-Methylimidazol-1-yl)-3-trifluoromethylphenylamine 630126-05-5P, 2-Methyl-1-(4-nitro-2-trifluoromethylphenyl)-1H-imidazole 630126-07-7P, [6-(4-Amino-2-methylphenoxy)pyrimidin-4-yl]methylamine 630126-09-9P, [3-Methyl-4-(6-methylaminopyrimidin-4-yloxy)phenyl]carbamic acid benzyl ester 630126-11-3P, [4-(6-Chloropyrimidin-4-yloxy)-3-methylphenyl]carbamic acid benzyl ester 630126-12-4P, (4-Hydroxy-3-methylphenyl)carbamic acid benzyl ester 630126-13-5P, 6-(4-Aminobenzyl)pyrimidin-4-ylamine 630126-14-6P, [4-(6-Aminopyrimidin-4-ylmethyl)phenyl]carbamic acid tert-butyl ester 630126-15-7P, [4-(6-Azidopyrimidin-4-ylmethyl)phenyl]carbamic acid tert-butyl ester 630126-16-8P, 5-(6-Chloropyrimidin-4-yloxy)-1H-indole 630126-17-9P, 5-(6-Chloropyrimidin-4-yloxy)-2,3-dihydro-1H-indole

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of diarylurea derivs. useful for the treatment of
protein kinase dependent diseases and proliferative diseases)

IT 228400-22-4P 228400-61-1P 228400-77-9P
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630122-90-6P 630122-91-7P 630122-92-8P 630122-93-9P
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630123-15-8P, N-[4-(6-Chloropyrimidin-4-yloxy)phenyl]-N'-(4-chloro-3-trifluoromethylphenyl)urea 630123-16-9P, N-[4-(4-Methylaminopyrimidin-6-yloxy)phenyl]-N'-(4-tert-butylphenyl)urea 630123-18-1P,
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630123-20-5P, N-[4-(4-Aminopyrimidin-6-yloxy)phenyl]-N'-(4-chloro-3-trifluoromethylphenyl)urea 630123-22-7P 630123-24-9P,
N-[4-(6-Chloropyrimidin-4-yloxy)phenyl]-N'-[4-(4-ethylpiperazin-1-yl)-3-methoxyphenyl]urea 630123-26-1P, N-[4-(4-Chloropyrimidin-6-yloxy)phenyl]-N'-[3-methoxy-4-(piperidin-1-ylmethyl)phenyl]urea 630123-28-3P
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630125-27-8P 630125-28-9P 630125-29-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diarylurea derivs. useful for the treatment of protein kinase dependent diseases and proliferative diseases)

L110 ANSWER 36 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:796477 HCAPLUS Full-text
DOCUMENT NUMBER: 139:307759
TITLE: Preparation of substituted benzazoles as Raf kinase inhibitors
INVENTOR(S): Renhowe, Paul A.; Ramurthy, Savithri; Amiri, Payman; Levine, Barry Haskell; Poon, Daniel J.; Subramanian, Sharadha; Sung, Leonard; Fantl, Wendy
PATENT ASSIGNEE(S): Chiron Corporation, USA
SOURCE: PCT Int. Appl., 259 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082272	A1	20031009	WO 2003-US10117	20030331 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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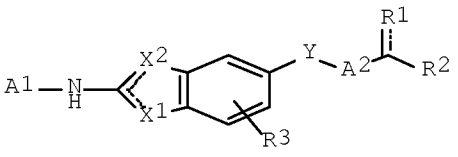
AU 2003226211	A1	20031013	AU 2003-226211	20030331 <--
AU 2003226211	B2	20080529		

EP 1499311	A1	20050126	EP 2003-745683	20030331 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008854	A	20050222	BR 2003-8854	20030331 <--
CN 1655779	A	20050817	CN 2003-812193	20030331 <--
JP 2005529089	T	20050929	JP 2003-579810	20030331 <--
NZ 535985	A	20070427	NZ 2003-535985	20030331 <--
IN 2004KN01433	A	20051230	IN 2004-KN1433	20040927 <--
MX 2004PA09541	A	20050125	MX 2004-PA9541	20040929 <--
NO 2004004617	A	20041228	NO 2004-4617	20041026 <--
ZA 2004008386	A	20060531	ZA 2004-8386	20060308 <--
JP 2006193533	A	20060727	JP 2006-96143	20060330 <--

PRIORITY APPLN. INFO.:
US 2002-369066P P 20020329 <--
JP 2003-579810 A3 20030331 <--
WO 2003-US10117 W 20030331 <--

OTHER SOURCE(S): MARPAT 139:307759

GI



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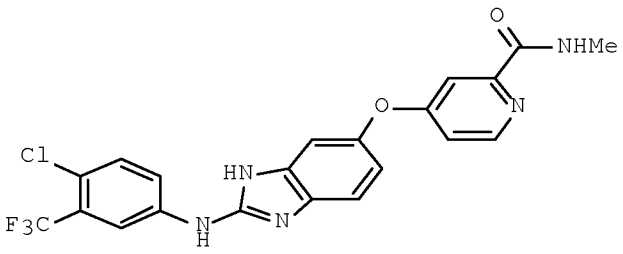


II

AB The title compds. [I; X1, X2 = N, NR4, O, S (with the provisos); Y = O, S; A1 = (un)substituted alkyl, cycloalkyl, aryl, etc.; A2 = (un)substituted heteroaryl; R1 = O, H, and R2 = NR5R6, OH; or CR1R2 = (un)substituted heterocycloalkyl, heteroaryl; R3 = H, halo, alkyl, alkoxy; R4 = H, OH, (di)alkylamino, alkyl; R5, R6 = H, (un)substituted alkyl, alkoxyalkyl, etc.; or R5 and R6 are taken together to form (un)substituted heterocyclyl or heteroaryl], useful for inhibition of Raf kinase activity in a human or animal subject, were prepared E.g., a 3-step synthesis of the benzimidazole II (starting from 4-amino-3-nitrophenol and (4-chloropyridin-2-yl)-N-methylcarboxamide), was given. The compds. of examples 1-1094 showed a Raf kinase inhibitory activity at an IC50 of less than 5 μM. A composition comprising the compound I is claimed. The new compds. compns. may be used either alone or in combination with at least one addnl. agent for the treatment of a Raf kinase mediated disorder, such as cancer.

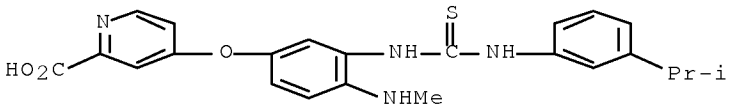
IT 611225-97-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted benzazoles as Raf kinase inhibitors)

RN 611225-97-9 HCAPLUS

CN 2-Pyridinecarboxylic acid, 4-[4-(methylamino)-3-[[[[3-(1-methylethyl)phenyl]amino]thioxomethyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM A61K031-41
ICS C07D401-12; C07D405-14; C07D409-14; C07D401-14; C07D417-12; C07D417-14; C07D413-14; C07D407-14; C07D413-12; C07D471-08; A61P035-00

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 823-54-1P 3530-00-5P, 3-Phenoxyphenylisothiocyanate 7748-59-6P 7748-60-9P 20734-76-3P 23491-48-7P 49559-34-4P 49559-83-3P 54998-08-2P 106146-35-4P 114780-06-2P 115619-00-6P 115619-01-7P 120381-42-2P 129488-00-2P 210158-20-6P 211635-75-5P 214337-39-0P 219552-64-4P 220000-86-2P 262368-47-8P 284462-57-3P 284462-58-4P 401815-98-3P 402948-23-6P 402948-25-8P 402948-26-9P 414880-35-6P 483324-01-2P 485841-45-0P 485841-46-1P 485841-47-2P 485841-49-4P 611225-42-4P 611225-43-5P 611225-44-6P 611225-45-7P 611225-46-8P 611225-52-6P 611225-53-7P 611225-54-8P 611225-58-2P 611225-59-3P 611225-60-6P 611225-61-7P 611225-62-8P 611225-63-9P 611225-64-0P 611225-65-1P 611225-66-2P 611225-67-3P 611225-68-4P 611225-69-5P 611225-70-8P 611225-71-9P 611225-72-0P 611225-73-1P 611225-74-2P 611225-75-3P 611225-76-4P 611225-77-5P 611225-78-6P 611225-79-7P 611225-80-0P 611225-81-1P 611225-82-2P 611225-83-3P 611225-84-4P 611225-85-5P 611225-86-6P 611225-87-7P 611225-88-8P 611225-89-9P 611225-90-2P 611225-91-3P 611225-92-4P 611225-93-5P 611225-94-6P 611225-95-7P 611225-96-8P 611225-97-9P 611225-98-0P 611225-99-1P 611226-00-7P 611226-01-8P 611226-02-9P 611226-03-0P 611226-04-1P 611226-05-2P 611226-06-3P 611226-07-4P 611226-08-5P 611226-09-6P 611226-11-0P 611226-12-1P 611226-13-2P 611226-14-3P 611226-15-4P 611226-17-6P 611226-18-7P 611226-19-8P 611226-20-1P 611226-21-2P 611226-22-3P 611226-23-4P 611226-24-5P 611226-25-6P 611226-26-7P 611226-27-8P 611226-28-9P 611226-29-0P 611226-30-3P 611226-31-4P 611226-32-5P 611226-33-6P 611226-34-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted benzazoles as Raf kinase inhibitors)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 37 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737931 HCAPLUS Full-text
DOCUMENT NUMBER: 139:255332
TITLE: Method for selecting antitumor drug sensitivity-determining factors and method for predicting antitumor drug sensitivity using the selected factors
INVENTOR(S): Aoki, Yuko; Hasegawa, Kiyoshi; Ishii, Nobuya; Mori, Kazushige
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2

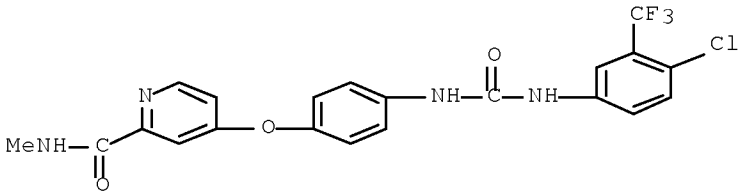
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076660	A1	20030918	WO 2002-JP2354	20020313 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2478640	A1	20030918	CA 2002-2478640	20020313 <--
AU 2002238874	A1	20030922	AU 2002-238874	20020313 <--
EP 1483401	A1	20041208	EP 2002-705127	20020313 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1625602	A	20050608	CN 2002-828958	20020313 <--
JP 2005519610	T	20050707	JP 2003-574857	20020313 <--
US 20050118600	A1	20050602	US 2005-507389	20050120 <--
PRIORITY APPLN. INFO.:			WO 2002-JP2354 W	20020313 <--

AB Based on drug sensitivity data and extensive gene expression data, a model was constructed by multivariate anal. with the partial least squares method type 1. Further, the model was optimized using modeling power and genetic algorithm. Thereby, the degree of contribution of the resp. genes to drug sensitivity was determined to select genes with a high degree of contribution. In addition, the levels of gene expression in specimens were analyzed, and then the drug sensitivity was predicted based on the model. The predicted values agreed well with those drug sensitivity values determined exptl. The drug sensitivity-predicting method provided by the present invention enables assessment of the effectiveness of a drug prior to administration using small quantities of specimens associated with diseases such as cancer. Since this enables the selection of the most suitable drug for each patient, the present invention is very useful in improving a patient's quality of life (QOL).

IT 284461-73-0, BAY 439006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for selecting antitumor drug sensitivity-determining factors and predicting antitumor drug sensitivity using the selected factors)

RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C12Q001-68
ICS G06K009-62; G06F017-17
CC 1-6 (Pharmacology)
Section cross-reference(s): 2
IT 51-21-8, 5-FU 66-22-8, 2,4(1H,3H)-Pyrimidinedione, biological studies 147-94-4, Ara-C 2207-75-2, Potassium oxonate 2353-33-5, Decitabine 3094-09-5, Furtulon 4291-63-8, Cladribine 7689-03-4, Camptothecin 10540-29-1, Tamoxifen 15663-27-1, Cisplatin 17902-23-7, Tegafur 20830-81-3, Daunomycin 25316-40-9, Adriamycin 33069-62-4, Taxol 41575-94-4, Carboplatin 53714-56-0, Leuprorelin 56420-45-2, Epirubicin 58957-92-9, Idarubicin 61422-45-5, Carmofur 75607-67-9 82640-04-8, LY156758 90357-06-5, ZD 176334 91421-42-0, 9-Nitrocamptothecin 91421-43-1, 9-Aminocamptothecin 100286-90-6, CPT-11 103766-25-2, 5-Chloro-2,4-dihydroxypyridine 105149-00-6, TZP4238 107868-30-4, FCE24304 110417-88-4, Dolastatin 10 112809-51-5, CGS 20267 114977-28-5, Taxotere 115767-74-3, TAT59 119804-96-5, DMDC 120511-73-1, ZD 1033 120685-11-2, CGP41251 123884-00-4, Dolastatin 15 123948-87-8, Topotecan 126723-15-7, Dolastatin 14 145918-75-8, Troxacitabine 149606-27-9, TZT 1027 154361-50-9, Xeloda 159776-69-9, Cemadotin 160237-25-2, BMS 184476 169869-90-3, DX-8951f 171179-06-9, PD 158780 172481-83-3, BMS 188797 172903-00-3, BBR 3464 182133-25-1, LY353381 182167-03-9, EM800 183319-69-9, CP 358774 184475-35-2, ZD 1839 186348-23-2, IDN 5109 189453-10-9, Epothilone D 192185-68-5, R115777 193275-84-2, SCH66336 195987-41-8, BMS 214662 204005-46-9, SU5416 212142-18-2, PTK787 212631-79-3, CI1040 219989-84-1, BMS 247550 220127-57-1, STI-571 220997-97-7, BN-80915 252916-29-3, SU6668 253863-00-2, L778123 284461-73-0, BAY 439006 437755-78-7, GW 2016 443913-73-3, ZD6474 601517-74-2, GW 2286
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for selecting antitumor drug sensitivity-determining factors and predicting antitumor drug sensitivity using the selected factors)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 38 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:656745 HCAPLUS Full-text
DOCUMENT NUMBER: 139:197377
TITLE: Preparation of aryl ureas for therapeutic use as kinase inhibitors
INVENTOR(S): Dumas, Jacques; Scott, William J.; Chien, Du-Schieng; Lee, Wendy; Bjorge, Susan; Musza, Laszlo L.; Nassar, Ala; Riedl, Bernd
PATENT ASSIGNEE(S): Bayer Corporation, USA; Bayer Pharmaceuticals Corporation
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068746	A1	20030821	WO 2003-US4109	20030211 <--
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            PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
            UG, US, UZ, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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            FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    CA 2475818          A1    20030821    CA 2003-2475818        20030211 <--
    AU 2003209118       A1    20030904    AU 2003-209118         20030211 <--
    US 20030216446      A1    20031120    US 2003-361859         20030211 <--
    EP 1474393          A1    20041110    EP 2003-707848         20030211 <--
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            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
    CN 1630638          A     20050622    CN 2003-803705         20030211 <--
    JP 2005523278       T     20050804    JP 2003-567877         20030211 <--
    EP 1580188          A1    20050928    EP 2005-7027           20030211 <--
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, FI, CY, TR, BG, CZ, EE, HU, SK
    MX 2004PA07830      A     20050701    MX 2004-PA7830         20040811 <--
    HK 1079774          A1    20071221    HK 2005-111827         20051222 <--
PRIORITY APPLN. INFO.:                    US 2002-354937P     P  20020211 <--
                                          EP 2003-707848      A3 20030211 <--
                                          WO 2003-US4109      W  20030211 <--
OTHER SOURCE(S):        MARPAT 139:197377
GI
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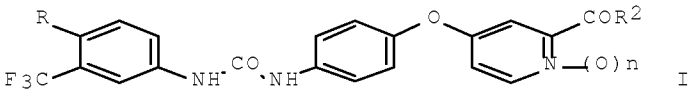


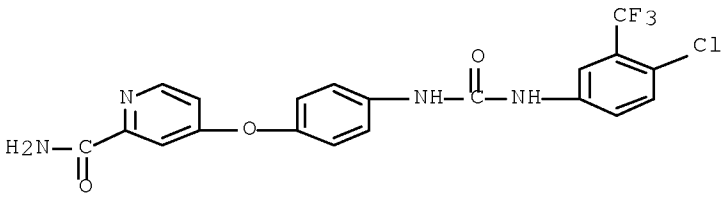
I

AB Aryl ureas, such as I [R = Cl, Br; R2 = OH, NH2, NHMe, NHCH2OH, alkoxy; n = 0, 1], were prepared for use in pharmaceutical compns. for the treatment of raf kinase and p38 kinase mediated diseases. These ureas are useful for the treatment of inflammation, osteoporosis, angiogenesis disorders and hyper-proliferative disorders, such as cancer. Thus, urea I (R = Cl, R2 = NHMe, n = 1) was prepared with 57% yield by N-oxidation of I (R = Cl, R2 = NHMe, n = 0) using 3-chloroperbenzoic acid in CH2Cl2 and THF. The prepared ureas were assayed for inhibition of p38 kinase and raf kinase, as well as for cancer cell growth inhibition in human cancer cell lines, such as HCT116 and DLD-1.

IT 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-carbamoyl(4-pyridyloxy)phenyl]urea
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aryl ureas for therapeutic use as kinase inhibitors)

RN 284461-74-1 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]- (CA INDEX NAME)



IC ICM C07D213-79
ICS C07D213-81; C07D213-89; A61K031-44; A61P011-00; A61P019-00; A61P025-00; A61P029-00
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
IT 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-carbamoyl(4-pyridyloxy)phenyl]urea 284462-18-6P 583840-03-3P 583840-04-4P 583840-09-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aryl ureas for therapeutic use as kinase inhibitors)
IT 583840-05-5P 583840-06-6P 583840-07-7P 583840-08-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl ureas for therapeutic use as kinase inhibitors)
IT 99586-65-9P, 4-Chloro-2-pyridinecarboxamide 284461-73-0P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)(4-pyridyloxy)phenyl]urea 284462-80-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aryl ureas for therapeutic use as kinase inhibitors)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 39 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:656581 HCAPLUS Full-text
DOCUMENT NUMBER: 139:197370
TITLE: Preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors
INVENTOR(S): Dumas, Jacques; Scott, William J.; Riedl, Bernd
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068229	A1	20030821	WO 2003-US4110	20030211 <--

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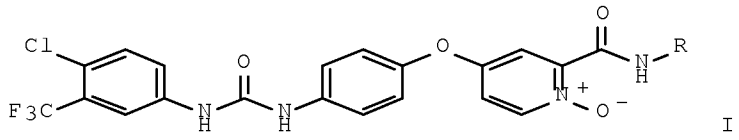
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003209119	A1	20030904	AU 2003-209119		20030211 <--
US 20030216396	A1	20031120	US 2003-361850		20030211 <--
US 20070265315	A1	20071115	US 2007-775457		20070710 <--
PRIORITY APPLN. INFO.:			US 2002-354935P	P	20020211 <--
			US 2003-361850	B1	20030211 <--
			WO 2003-US4110	W	20030211 <--

OTHER SOURCE(S): MARPAT 139:197370
GI

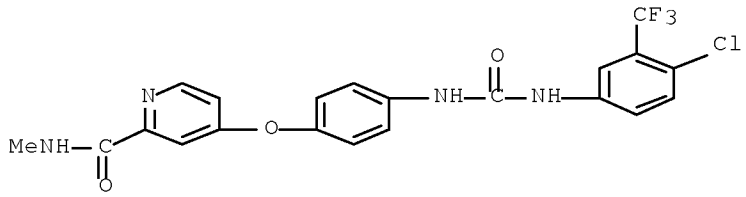


I

AB The title ureas containing a pyridine, quinoline, or isoquinoline functionality which is oxidized at the nitrogen heteroatom MLBNHCONHA [A = (un)substituted Ph, naphthyl, 5-6 membered monocyclic heteroaryl, 8-10 membered bicyclic heteroaryl; B = (un)substituted phenylene, naphthylene, 5-6 membered monocyclic heteroarylene, 8-10 membered bicyclic heteroarylene; L = (CH2)mO(CH2)l, (CH2)m(CH2)l, (CH2)mCO(CH2)l, etc.; m, l = 0-4; M = (un)substituted pyridine-1-oxide, quinoline-1-oxide, isoquinoline-1-oxide; with the provisos] which are useful in the treatment of (i) raf mediated diseases, for example, cancer, (ii) p38 mediated diseases such as inflammation and osteoporosis, and (iii) VEGF mediated diseases such as angiogenesis disorders, were claimed. Preparation of two ureas such as I [R = H, Me] which are not compds. of the invention, and have been distinguished from the compds. of the invention by a proviso, was described. Pharmaceutical composition comprising the title ureas was claimed.

IT 284461-73-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors)

RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-44
ICS A61K031-47; C07D213-89; C07D215-60; C07D217-08; A61P035-00; A61P029-00
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
IT 123-30-8, 4-Aminophenol 320-51-4 176977-85-8, Methyl 4-chloro-2-pyridinecarboxylate hydrochloride 284461-73-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors)
IT 99586-65-9P 284461-74-1P 284462-80-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors)
IT 583840-03-3P 583840-04-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 40 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:656580 HCAPLUS Full-text
DOCUMENT NUMBER: 139:197369
TITLE: Preparation of aryl ureas with angiogenesis inhibiting activity
INVENTOR(S): Dumas, Jacques; Scott, William J.; Elting, James; Hatoum-Makdad, Holia
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068228	A1	20030821	WO 2003-US4103	20030211 <--
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475703	A1	20030821	CA 2003-2475703	20030211 <--
AU 2003209116	A1	20030904	AU 2003-209116	20030211 <--
US 20030207870	A1	20031106	US 2003-361858	20030211 <--
EP 1478358	A1	20041124	EP 2003-707846	20030211 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005522448	T	20050728	JP 2003-567410	20030211 <--
MX 2004PA07832	A	20050908	MX 2004-PA7832	20040811 <--

JP 2007302687 A 20071122 JP 2007-183948 20070713 <--
PRIORITY APPLN. INFO.: US 2002-354950P P 20020211 <--
JP 2003-567410 A3 20030211 <--
WO 2003-US4103 W 20030211 <--
OTHER SOURCE(S): MARPAT 139:197369
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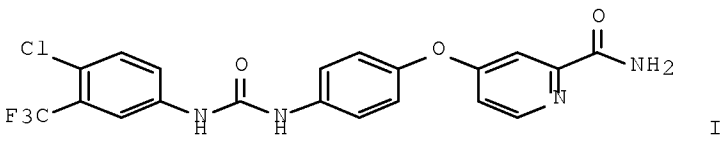

I

AB The title compds. ANHCONHB [A, B = (un)substituted Ph, naphthyl, 5-6 membered monocyclic heteroaryl, etc.], useful for treating diseases mediated by the VEGF induced signal transduction pathway characterized by abnormal angiogenesis or hyperpermeability processes, were claimed. Prepns. of three title ureas are described. E.g., a 3-step synthesis of the urea I (starting from Me 4-chloro-2-pyridinecarboxylate hydrochloride), was given. The KDR (VEGFR2) assay for testing the title ureas is described.

IT 284461-44-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl ureas with angiogenesis inhibiting activity)

RN 284461-44-5 HCAPLUS
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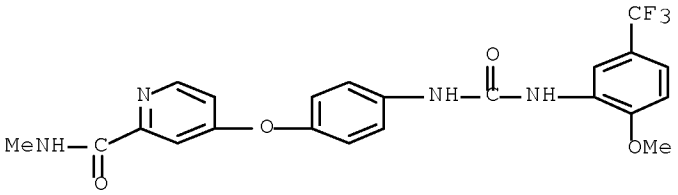

IC ICM A61K031-44
ICS A61K031-4436; A61K031-4725; A61K031-4709; A61K031-17; A61P035-00; A61P017-06; A61P019-02; A61P027-02

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT 284461-44-5P 284461-73-0P 284461-74-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl ureas with angiogenesis inhibiting activity)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 41 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:633416 HCAPLUS Full-text
DOCUMENT NUMBER: 139:173786
TITLE: Method for treating diseases associated with abnormal kinase activity
INVENTOR(S): Lyons, John; Rubinfeld, Joseph
PATENT ASSIGNEE(S): Supergen, Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003065995	A2	20030814	WO 2003-US3537	20030206 <--
WO 2003065995	A3	20051013		
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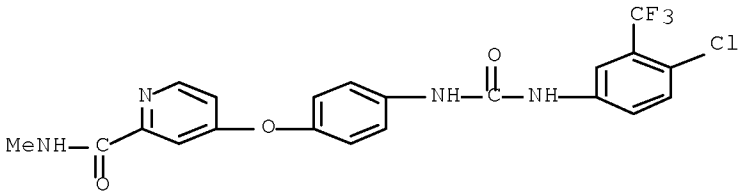
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20030147813	A1	20030807	US 2002-71849	20020207 <--
US 20040127453	A1	20040701	US 2002-206854	20020726 <--
US 6998391	B2	20060214		
CA 2474174	A1	20030814	CA 2003-2474174	20030206 <--
AU 2003215065	A1	20030902	AU 2003-215065	20030206 <--
EP 1572075	A2	20050914	EP 2003-710881	20030206 <--
EP 1572075	A3	20051207		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:
US 2002-71849 A1 20020207 <--
US 2002-206854 A1 20020726 <--
WO 2003-US3537 W 20030206 <--

AB Methods are provided for treating diseases associated with abnormal activity of kinases such as chronic myelogenous leukemia. The method comprises: administering a DNA methylation inhibitor to the patient in therapeutically effective amount; and administering a kinase inhibitor such as imatinib mesylate to the patient in therapeutically effective amount, such that the in vivo activity of the kinase is reduced relative to that prior to the treatment. The method can be used to treat cancer associated with abnormal activity of kinases such as phosphatidylinositol 3'-kinase (P13K), protein kinases including serine/threonine kinases such as Raf kinases, protein kinase kinases such as MEK, and tyrosine kinases such as those in the epidermal growth factor receptor family (EGFR), platelet-derived growth factor receptor family (PDGFR), vascular endothelial growth factor receptor (VEGFR) family, nerve growth factor receptor family (NGFR), fibroblast growth factor receptor family (FGFR) insulin receptor family, ephrin receptor family, Met family, Ror family, c-kit family, Src family, Fes family, JAK family, Fak family, Btk family, Syk/ZAP-70 family, and Abl family.

IT 284461-73-0, BAY 43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of diseases associated with abnormal kinase activity with

serine/threonine kinase inhibitor and DNA methylation inhibitor)
RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K
CC 1-6 (Pharmacology)
IT 109511-58-2, U0126 154447-36-6, LY294002 167869-21-8, PD98059
212631-79-3, PD184352 284461-73-0, BAY 43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of diseases associated with abnormal kinase activity with serine/threonine kinase inhibitor and DNA methylation inhibitor)

L110 ANSWER 42 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:454119 HCAPLUS Full-text
DOCUMENT NUMBER: 139:17567
TITLE: Aryl urea compounds in combination with other cytostatic or cytotoxic agents for treating human cancers and other raf kinase-mediated diseases
INVENTOR(S): Carter, Christopher A.; Dumas, Jacques; Gibson, Neil; Hibner, Barbara; Humphrey, Rachel W.; Trail, Pamela; Vincent, Patrick W.; Zhai, Yifan; Riedl, Bernd; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.
PATENT ASSIGNEE(S): Bayer Corporation, USA; Bayer AG
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003047579	A1	20030612	WO 2002-US38439	20021203 <--

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2468463	A1	20030612	CA 2002-2468463	20021203 <--
AU 2002351196	A1	20030617	AU 2002-351196	20021203 <--
US 20030232765	A1	20031218	US 2002-308187	20021203 <--
EP 1450799	A1	20040901	EP 2002-786842	20021203 <--
EP 1450799	B1	20061115		
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JP 2005511658	T	20050428	JP 2003-548834	20021203 <--
AT 345130	T	20061215	AT 2002-786842	20021203 <--
EP 1769795	A2	20070404	EP 2006-23696	20021203 <--
EP 1769795	A3	20080312		
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ES 2275931	T3	20070616	ES 2002-786842	20021203 <--
RU 2316326	C2	20080210	RU 2004-120785	20021203 <--
IN 2004DN01420	A	20070316	IN 2004-DN1420	20040526 <--
MX 2004PA05137	A	20050603	MX 2004-PA5137	20040528 <--
ZA 2004004225	A	20050829	ZA 2004-4225	20040528 <--
US 20060247186	A1	20061102	US 2006-480360	20060705 <--

PRIORITY APPLN. INFO.:	US 2001-334609P	P	20011203 <--
	EP 2002-786842	A3	20021203 <--
	US 2002-308187	B1	20021203 <--
	WO 2002-US38439	W	20021203 <--

OTHER SOURCE(S): MARPAT 139:17567

AB The invention discloses aryl urea compds. in combination with cytotoxic or cytostatic agents for use in treating raf kinase-mediated diseases, e.g. cancer.

IT 475207-59-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aryl urea compds. in combination with other cytostatic or cytotoxic agents for treating human cancers and other raf kinase-mediated diseases)

RN 475207-59-1 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-, 4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 284461-73-0
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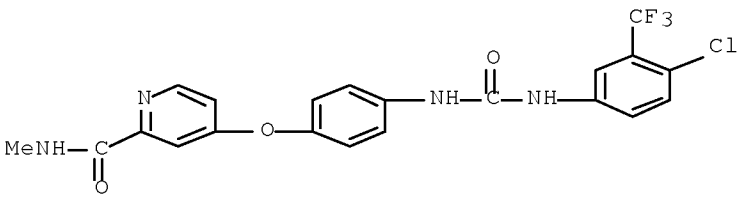
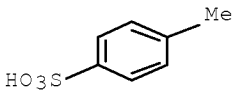


CM 2

CRN 104-15-4

CMF C7 H8 O3 S



IC ICM A61K031-44
ICS A61K031-535; A61K031-65; A61K031-435; A61K031-505; A61K031-47
CC 1-6 (Pharmacology)
IT 50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 50-76-0, Actinomycin D 51-21-8, 5-Fluorouracil 57-13-6D, Urea, aryl derivs. 57-22-7, Vincristine 59-05-2, Methotrexate 147-94-4, AraC 148-82-3, Melphalan 154-93-8, BCNU 865-21-4, Vinblastine 4342-03-4, DTIC 5536-17-4, AraA 13010-47-4, CCNU 15663-27-1, Cisplatin 23214-92-8, Doxorubicin 25316-40-9, Doxorubicin hydrochloride 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin 71486-22-1, Vinorelbine 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 114977-28-5, Taxotere 122111-03-9, Gemzar 125317-39-7, Navelbine 180288-69-1, Herceptin 184475-35-2, Gefitinib 475207-59-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aryl urea compds. in combination with other cytostatic or cytotoxic agents for treating human cancers and other raf kinase-mediated diseases)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 43 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:454071 HCAPLUS Full-text
DOCUMENT NUMBER: 139:30782
TITLE: RAF-MEK-ERK pathway inhibitors to treat cancer
INVENTOR(S): Lyons, John F.; Bollag, Gideon
PATENT ASSIGNEE(S): Onyx Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003047523	A2	20030612	WO 2002-US38402	20021203 <--
WO 2003047523	A3	20060223		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2466762	A1	20030612	CA 2002-2466762	20021203 <--
AU 2002365899	A1	20030617	AU 2002-365899	20021203 <--

AU 2002365899	B2	20070913			
US 20030125359	A1	20030703	US 2002-308721	20021203	<--
US 7307071	B2	20071211			
JP 2005526008	T	20050902	JP 2003-548784	20021203	<--
EP 1578346	A2	20050928	EP 2002-804478	20021203	<--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

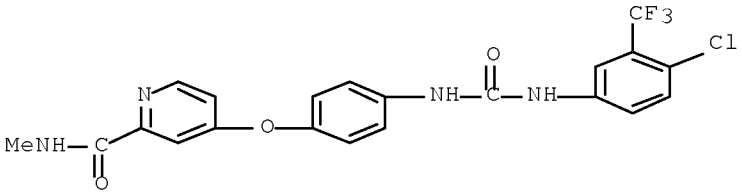
PRIORITY APPLN. INFO.: US 2001-336886P P 20011204 <--
WO 2002-US38402 W 20021203 <--

AB Materials and methods for treating certain cancers are described, preferably cancers that result from the up-regulation of the RAF-MEK-ERK pathway, and more preferably chronic myelogenous leukemia, and which cancer is preferably resistant to the inhibitor of Bcr-Abl tyrosine kinase, imatinib.

IT 284461-73-0, BAY 43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAY 43-9006; RAF-MEK-ERK pathway inhibitors to treat cancer)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K

CC 1-6 (Pharmacology)

IT 284461-73-0, BAY 43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAY 43-9006; RAF-MEK-ERK pathway inhibitors to treat cancer)

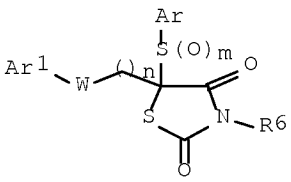
L110 ANSWER 44 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:173484 HCAPLUS Full-text
DOCUMENT NUMBER: 138:221581
TITLE: Method of using 5-(arylsulfonyl), 5-(arylsulfinyl) and 5-(arylsulfanyl)thiazolidine-2,4-diones for inhibition of farnesyl-protein transferase
INVENTOR(S): Ayral-kaloustian, Semiramis; Epstein, Joseph William; Birnberg, Gary Harold; Salaski, Edward James; Macewan, Gloria Jean; Cheung, Katherine
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003018135	A1	20030306	WO 2002-US26691	20020822 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002356135	A1	20030310	AU 2002-356135	20020822 <--
US 20030144301	A1	20030731	US 2002-226815	20020823 <--
US 6605628	B2	20030812		
US 20030149063	A1	20030807	US 2002-227084	20020823 <--
US 6784184	B2	20040831		
PRIORITY APPLN. INFO.:			US 2001-314586P	P 20010824 <--
			US 2001-314621P	P 20010824 <--
			WO 2002-US26691	W 20020822 <--

OTHER SOURCE(S): MARPAT 138:221581

GI



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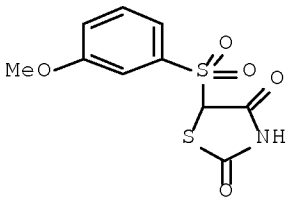


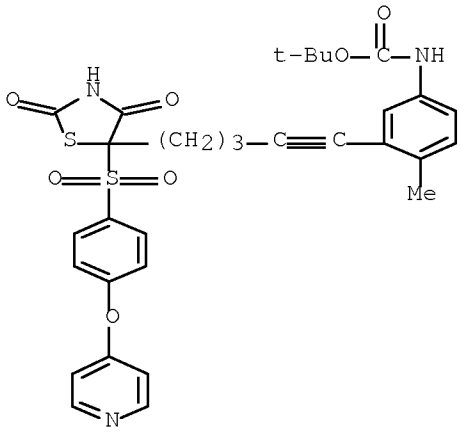
II

AB Title compds. I [Ar = naphthyl, quinolinyl, thienyl, pyridinyl, etc.; m = 0-2; R6 = H, alkyl, benzyl, etc.; W = C.tplbond.C, E/Z-CH=CH, CONH, etc.; n = 1-9; Ar1 = thienyl, pyridinyl, etc.] are prepared For instance, 5-bromothiazolidine-2,4-dione is reacted with 3-methoxybenzenethiol (THF, NaHMDS, -78°-room temperature); the intermediate sulfanyl derivative is oxidized (HOAc, H2O2) to give II. I are inhibitors of Ras FPTase, and may be used as an alternative to, or in conjunction with, traditional cancer therapy for treating ras-oncogene-dependent tumors, such as cancers of the pancreas, colon, bladder, and thyroid.

IT 500710-93-0P, tert-Butyl [3-[5-[2,4-dioxo-5-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of using 5-(arylsulfonyl), 5-(arylsulfinyl) and 5-(arylsulfanyl)thiazolidine-2,4-diones for inhibition of farnesyl-protein transferase)

RN 500710-93-0 HCAPLUS

CN Carbamic acid, [3-[5-[2,4-dioxo-5-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-5-thiazolidinyl]-1-pentynyl]-4-methylphenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IC ICM A61P035-00
CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
IT 125518-56-1P, 5-(4-Fluorophenylsulfonyl)thiazolidine-2,4-dione
125540-45-6P 173019-14-2P, 5-[3-(4-Chlorophenyl)-2-propynyl]-5-[(4-methylphenyl)sulfonyl]thiazolidine-2,4-dione 173019-20-0P, 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(4-fluorobenzenesulfonyl)thiazolidine-2,4-dione 173019-22-2P, 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(naphthalene-2-sulfonyl)thiazolidine-2,4-dione 173019-23-3P, 5-Benzenesulfonyl-5-[3-(4-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-24-4P, 5-Benzenesulfonyl-5-(3-phenylprop-2-ynyl)thiazolidine-2,4-dione 173019-26-6P, 5-(4-Chlorobenzenesulfonyl)-5-(3-phenylprop-2-ynyl)thiazolidine-2,4-dione 173019-27-7P, 5-(4-Chlorobenzenesulfonyl)-5-[3-(4-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-29-9P, 5-(4-Bromobenzenesulfonyl)-5-[3-(4-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-31-3P, 5-[3-(4-Fluorophenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-33-5P, 5-(4-Toluenesulfonyl)-5-[3-(p-tolyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-34-6P, 5-(4-Bromobenzenesulfonyl)-5-(3-phenylprop-2-ynyl)thiazolidine-2,4-dione 173019-36-8P, 5-(Naphthalene-2-sulfonyl)-5-(3-phenylprop-2-ynyl)thiazolidine-2,4-dione 173019-38-0P, 5-(4-Toluenesulfonyl)-5-[3-(4-trifluoromethylphenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-40-4P, 5-[3-(4-Methoxyphenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-41-5P, 5-[3-(4-Bromophenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-43-7P, 5-Benzenesulfonyl-5-[3-(4-trifluoromethylphenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-45-9P, 5-(4-Chlorobenzenesulfonyl)-5-[3-(4-fluorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-46-0P, 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(toluene-3-sulfonyl)thiazolidine-2,4-dione 173019-47-1P, 5-[3-(3-Chlorophenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-49-3P, 5-Benzenesulfonyl-5-[3-(2-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-51-7P, 5-Benzenesulfonyl-5-[3-[3,5-bis(trifluoromethyl)phenyl]prop-2-ynyl]thiazolidine-2,4-dione 173019-52-8P, 5-[3-[3,5-Bis(trifluoromethyl)phenyl]prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 173019-53-9P, 5-Benzenesulfonyl-5-[3-(3-chlorophenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-56-2P, 5-(4-Fluorobenzenesulfonyl)-5-[3-(4-trifluoromethylphenyl)prop-2-ynyl]thiazolidine-2,4-dione 173019-62-0P, 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(quinoline-2-

sulfonyl)thiazolidine-2,4-dione 204848-63-5P, 5-[3-(4-Chlorophenyl)prop-2-ynyl]-5-(p-tolylsulfanyl)thiazolidine-2,4-dione 204848-70-4P, 5-[3-(4-Bromophenyl)prop-2-ynyl]-5-(4-chlorobenzenesulfonyl)thiazolidine-2,4-dione 500708-44-1P, 5-(3-Methoxyphenylsulfonyl)thiazolidine-2,4-dione 500708-46-3P, 5-(4-Iodophenylsulfonyl)thiazolidine-2,4-dione 500708-48-5P, 5-((4-(Trifluoromethoxy)benzene)sulfonyl)thiazolidine-2,4-dione 500708-49-6P, 5-(3-Nitrobenzenesulfonyl)thiazolidine-2,4-dione 500708-54-3P, 5-(4-Nitrobenzenesulfonyl)thiazolidine-2,4-dione 500708-60-1P, 5-[[4-((Pyridin-4-yl)oxy)benzene]sulfonyl]thiazolidine-2,4-dione 500708-65-6P, 5-(4-Phenoxybenzensulfonyl)thiazolidine-2,4-dione 500708-67-8P, 5-(4-Benzyloxybenzenesulfonyl)thiazolidine-2,4-dione 500708-70-3P, 5-(3,4-Dimethoxybenzenesulfonyl)thiazolidine-2,4-dione 500708-73-6P, N-[5-((2,4-Dioxothiazolidine-5-yl)sulfonyl)-2-methoxyphenyl]acetamide 500708-78-1P, 5-(5-Chlorothiophene-2-sulfonyl)thiazolidine-2,4-dione 500708-81-6P, 5-(Thiophene-2-sulfonyl)thiazolidine-2,4-dione 500708-85-0P, 5-(5-(Pyridin-2-yl)thiophene-2-sulfonyl)thiazolidine-2,4-dione 500708-93-0P, 5-(4-Butoxybenzenesulfonyl)thiazolidine-2,4-dione 500709-00-2P 500709-82-0P, 5-(4-Methoxyphenylsulfanyl)-5-(5-(thiophen-2-yl)pentan-4-ynyl)thiazolidine-2,4-dione 500709-83-1P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-fluorophenylsulfanyl)thiazolidine-2,4-dione 500709-85-3P, 5-[6-(4-Chlorophenyl)hexan-5-ynyl]-5-(4-methoxyphenylsulfonyl)thiazolidine-2,4-dione 500709-86-4P, 5-[11-(4-Chlorophenyl)undecan-10-ynyl]-5-(4-methoxyphenylsulfonyl)thiazolidine-2,4-dione 500709-87-5P, 5-[5-(2-Chlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500709-88-6P, 5-[5-(3-Chlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500709-90-0P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-iodobenzenesulfonyl)thiazolidine-2,4-dione 500709-91-1P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-fluorobenzenesulfonyl)thiazolidine-2,4-dione 500709-92-2P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-phenoxybenzenesulfonyl)thiazolidine-2,4-dione 500709-93-3P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(naphthalene-2-sulfonyl)thiazolidine-2,4-dione 500709-94-4P, N-[4-[[5-[5-(4-Chlorophenyl)pentan-4-ynyl]-2,4-dioxothiazolidine-5-yl]sulfonyl]phenyl]acetamide 500709-95-5P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(quinoline-8-sulfonyl)thiazolidine-2,4-dione 500709-96-6P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-nitrobenzenesulfonyl)thiazolidine-2,4-dione 500709-97-7P, 5-(4-Benzyloxybenzenesulfonyl)-5-[5-(4-chlorophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500709-98-8P, 5-(4-Butoxybenzenesulfonyl)-5-[5-(4-chlorophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500709-99-9P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(naphthalene-1-sulfonyl)thiazolidine-2,4-dione 500710-01-0P, 5-[5-(2,5-Dichlorophenyl)pentan-4-ynyl]-5-(4-iodobenzenesulfonyl)thiazolidine-2,4-dione 500710-02-1P 500710-03-2P, 5-[5-(2,4-Dichlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-05-4P, 5-[5-(3-Nitrophenyl)pentan-4-ynyl]-5-(4-phenoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-06-5P, 5-(4-Iodobenzenesulfonyl)-5-[5-(4-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-07-6P, 5-(4-Methoxybenzensulfonyl)-5-[5-(4-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-08-7P, 5-(4-Methoxybenzensulfonyl)-5-[5-(2-methyl-5-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-09-8P 500710-10-1P, 5-[5-(2-Methyl-5-nitrophenyl)pentan-4-ynyl]-5-(4-phenoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-11-2P, 5-(4-Iodobenzenesulfonyl)-5-[5-(2-methyl-5-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-12-3P, 5-[5-(2-Methyl-5-nitrophenyl)pentan-4-ynyl]-5-(naphthalene-1-sulfonyl)thiazolidine-2,4-dione 500710-13-4P, 5-[5-(2-Methyl-5-nitrophenyl)pentan-4-ynyl]-5-(naphthalene-2-sulfonyl)thiazolidine-2,4-dione 500710-14-5P, 5-[5-(2-Methyl-4-nitrophenyl)pentan-4-ynyl]-5-[[4-((pyridin-4-

yl)oxy)benzene]sulfonyl]thiazolidine-2,4-dione 500710-15-6P, 5-[5-(2-Methyl-4-nitrophenyl)pentan-4-ynyl]-5-(4-phenoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-16-7P, 5-(4-Methoxybenzenesulfonyl)-5-[5-(2-methyl-4-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-17-8P, 5-(4-Iodobenzenesulfonyl)-5-[5-(2-methyl-4-nitrophenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-18-9P 500710-19-0P, 5-[5-(3-Fluoro-5-nitrophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-20-3P, 5-[5-(2,5-Dimethylphenyl)pentan-4-ynyl]-5-(4-iodobenzenesulfonyl)thiazolidine-2,4-dione 500710-21-4P, 5-[5-(2,5-Dimethylphenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-22-5P, 5-[5-(2,4-Dimethylphenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-23-6P, 5-[5-(2,4-Dimethylphenyl)pentan-4-ynyl]-5-(4-iodobenzenesulfonyl)thiazolidine-2,4-dione 500710-24-7P 500710-25-8P, 5-[5-(5-Chloro-2-methylphenyl)pentan-4-ynyl]-5-((4-trifluoromethoxybenzene)sulfonyl)thiazolidine-2,4-dione 500710-26-9P 500710-27-0P 500710-28-1P 500710-29-2P 500710-30-5P, 5-[5-(4-Bromo-2-methylphenyl)pentan-4-ynyl]-5-(4-iodobenzenesulfonyl)thiazolidine-2,4-dione 500710-31-6P, [4-[5-[5-(4-Methoxybenzensulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]phenyl]carbamic acid tert-Butyl Ester 500710-32-7P 500710-33-8P, N-tert-Butyl-3-[5-[5-(4-iodobenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylbenzamide 500710-34-9P, [3-[5-[5-(4-Iodobenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid tert-Butyl Ester 500710-35-0P, [4-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-3-methylphenyl]carbamic acid tert-Butyl Ester 500710-37-2P, [4-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-3-trifluoromethylphenyl]carbamic acid tert-Butyl Ester 500710-38-3P 500710-39-4P, 5-(4-Methoxybenzenesulfonyl)-5-[5-(4-trifluoromethylphenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-40-7P, 5-(4-Methoxybenzenesulfonyl)-5-[5-(4-trifluoromethoxyphenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-41-8P, 3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylbenzoic Acid Methyl Ester 500710-42-9P, 5-[5-(4-tert-Butylphenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-43-0P, 5-[5-(4-tert-Butylphenyl)pentan-4-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500710-44-1P, 4-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]benzonitrile 500710-45-2P, 5-[5-(4-(Methanesulfonyl)phenyl)pentan-4-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500710-47-4P, 5-(4-Methoxybenzenesulfonyl)-5-[5-(4-(pyrrol-1-yl)phenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-48-5P, 5-(4-Iodobenzenesulfonyl)-5-[5-(4-(pyrrol-1-yl)phenyl)pentan-4-ynyl]thiazolidine-2,4-dione 500710-49-6P, 5-[5-(4-(Pyrrol-1-yl)phenyl)pentan-4-ynyl]-5-((4-trifluoromethoxybenzene)sulfonyl)thiazolidine-2,4-dione 500710-50-9P, 5-(3-Methoxybenzenesulfonyl)-5-(5-(thiophen-2-yl)pentan-4-ynyl)thiazolidine-2,4-dione 500710-51-0P, 5-(4-Methylphenylsulfonyl)-5-(5-(thiophen-2-yl)pentan-4-ynyl)thiazolidine-2,4-dione 500710-52-1P, 5-(4-Methoxybenzenesulfonyl)-5-(5-(thiophen-2-yl)pentan-4-ynyl)thiazolidine-2,4-dione 500710-53-2P, 5-(4-Methoxybenzenesulfonyl)-5-(3-(pyridin-3-yl)prop-2-ynyl)thiazolidine-2,4-dione 500710-54-3P, 5-(3-(Thiophen-2-yl)prop-2-ynyl)-5-(toluene-4-sulfonyl)thiazolidine-2,4-dione 500710-55-4P, 5-(3-(1,1'-Biphenyl-4-yl)prop-2-ynyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500710-56-5P, 5-[3-(4-Phenoxyphenyl)prop-2-ynyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500710-57-6P, 5-(3-(1,1'-Biphenyl-4-yl)prop-2-ynyl)-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-59-8P, 5-(5-(Pyridin-3-yl)pentan-4-ynyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500710-60-1P, 5-[5-(5-Amino-2-methylphenyl)pentan-4-ynyl]-5-(4-

methoxybenzenesulfonyl)thiazolidine-2,4-dione 500710-61-2P, [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid Benzyl Ester 500710-62-3P 500710-63-4P, [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid 4-chlorophenyl Ester 500710-64-5P, [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid Methyl Ester 500710-65-6P, [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid isopropyl Ester 500710-66-7P, [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid Neopentyl Ester 500710-67-8P, [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-4-methylphenyl]carbamic acid Butyl Ester 500710-68-9P 500710-69-0P, N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-2-methylpropanamide 500710-70-3P, N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-3,3-dimethylbutanamide 500710-71-4P, N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-2,2-dimethylpropanamide 500710-72-5P, N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-2-phenylacetamide 500710-73-6P, N-Benzyl-N'-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]urea 500710-74-7P, N-(4-Methoxyphenyl)-N'-[3-(5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl)-4-methylphenyl]urea 500710-75-8P, N-(4-Chlorophenyl)-N'-[3-(5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl)-4-methylphenyl]urea 500710-76-9P, N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]-N'-(4-methylphenyl)urea 500710-77-0P, 4-Chloro-N-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]benzamide 500710-78-1P, 4-Methoxy-N-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]benzamide 500710-79-2P, N-[3-[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl][1,1'-biphenyl]-4-carboxamide 500710-80-5P, 4-(tert-Butyl)-N-[3-[5-[5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]benzamide 500710-81-6P, 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-[(5-chloro-2-thienyl)sulfonyl]-1,3-thiazolidine-2,4-dione 500710-82-7P, 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-(2-thienylsulfonyl)-1,3-thiazolidine-2,4-dione 500710-83-8P, 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-[(3,4-dimethoxyphenyl)sulfonyl]-1,3-thiazolidine-2,4-dione 500710-84-9P, 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-1,3-thiazolidine-2,4-dione 500710-85-0P, 5-[5-(4-Chlorophenyl)-4-pentynyl]-5-[[5-(2-pyridinyl)-2-thienyl]sulfonyl]-1,3-thiazolidine-2,4-dione 500710-86-1P, 5-[(5-Chloro-2-thienyl)sulfonyl]-5-[5-(2,5-dichlorophenyl)-4-pentynyl]-1,3-thiazolidine-2,4-dione 500710-87-2P, 5-[5-(2,5-Dichlorophenyl)-4-pentynyl]-5-(2-thienylsulfonyl)-1,3-thiazolidine-2,4-dione 500710-88-3P, 5-[5-(2,5-Dichlorophenyl)-4-pentynyl]-5-[(3,4-dimethoxyphenyl)sulfonyl]-1,3-thiazolidine-2,4-dione 500710-89-4P, 5-[5-(2,5-Dichlorophenyl)-4-pentynyl]-5-[[5-(2-pyridinyl)-2-thienyl]sulfonyl]-1,3-thiazolidine-2,4-dione 500710-90-7P, [3-[5-[5-[(5-Chloro-2-thienyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamic acid tert-butyl ester 500710-91-8P, tert-Butyl [3-[5-[2,4-dioxo-5-(2-thienylsulfonyl)-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate 500710-92-9P, tert-Butyl [3-[5-[5-[(3,4-dimethoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate 500710-93-0P, tert-Butyl [3-[5-[2,4-dioxo-5-[[4-(4-pyridinyloxy)phenyl]sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate 500710-94-1P, tert-Butyl [3-[5-[2,4-dioxo-5-[[5-

(2-pyridinyl)-2-thienyl]sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylphenyl]carbamate 500710-95-2P, N-(tert-Butyl)-3-[5-[5-[(5-chloro-2-thienyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylbenzamide 500710-96-3P, N-(tert-Butyl)-3-[5-[2,4-dioxo-5-(2-thienylsulfonyl)-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylbenzamide 500710-97-4P, N-(tert-Butyl)-3-(5-[5-[(3,4-dimethoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl)-4-methylbenzamide 500710-98-5P, N-(tert-Butyl)-3-[5-[2,4-dioxo-5-[[5-(2-pyridinyl)-2-thienyl]sulfonyl]-1,3-thiazolidin-5-yl]-1-pentynyl]-4-methylbenzamide 500710-99-6P, 4-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pent-1-ynyl]-3-methylbenzoic Acid 500711-00-2P, N-(4-Chlorobenzyl)-3-[5-(4-methoxyphenylsulfonyl)-2,4-dioxothiazolidin-5-yl]propionamide 500711-02-4P, N-[2-(4-Chlorophenyl)ethyl]-3-[5-(4-methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]propionamide 500711-03-5P, 5-[(4Z)-5-(4-Chlorophenyl)pent-4-enyl]-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500711-04-6P 500711-08-0P, 5-[3-(4-Chlorophenyl)propyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500711-09-1P, 5-[5-(3-Aminophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500711-10-4P, 5-(3-Phenylprop-2-enyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500711-11-5P 500711-12-6P 500711-13-7P, 5-(4-Methoxyphenylsulfinyl)thiazolidine-2,4-dione 500711-14-8P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-methoxyphenylsulfinyl)thiazolidine-2,4-dione 500711-15-9P, Benzyl 5-[5-[5-[[(benzyloxy)carbonyl]amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-16-0P, 4-Nitrobenzyl 5-[(4-methoxyphenyl)sulfonyl]-5-[5-[2-methyl-5-[[[(4-nitrobenzyl)oxy]carbonyl]amino]phenyl]pentan-4-ynyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-17-1P, Methyl 5-[5-[5-[(methoxycarbonyl)amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-18-2P, Isopropyl 5-[5-[5-[(isopropoxycarbonyl)amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-19-3P 500711-20-6P, Butyl 5-[5-[5-[(butoxycarbonyl)amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-21-7P, Isobutyl 5-[5-[5-[(isobutoxycarbonyl)amino]-2-methylphenyl]pentan-4-ynyl]-5-[(4-methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidine-3-carboxylate 500711-22-8P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-3-(3-(imidazol-1-yl)propyl)-5-(4-methoxybenzenesulfonyl)thiazolidine-2,4-dione 500711-24-0P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)-3-methylthiazolidine-2,4-dione 500711-25-1P, 3-(2,4-Diethoxybenzyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500711-26-2P, 5-[5-(4-Chlorophenyl)pentan-4-ynyl]-3-(2,4-diethoxybenzyl)-5-(4-toluenesulfonyl)thiazolidine-2,4-dione 500711-28-4P, 5-[5-(2,5-Dichlorophenyl)pentan-4-ynyl]-5-(4-methoxybenzenesulfonyl)-2,4-dioxothiazolidine-3-carboxylic acid 2-methoxyethyl ester 500711-31-9P, 5-[3-[3,5-Bis(trifluoromethyl)phenyl]prop-2-ynyl]thiazolidine-2,4-dione 500711-32-0P, [3-[5-[5-(4-Methoxybenzenesulfonyl)-2,4-dioxothiazolidin-5-yl]pentan-1-ynyl-4-methylphenyl]carbamic acid neopentyl ester 500711-33-1P, N-[3-[[5-[5-[(4-Methoxyphenyl)sulfonyl]-2,4-dioxo-1,3-thiazolidin-5-yl]-1-pentynyl]methyl]phenyl]-N'-(4-methylphenyl)urea

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(method of using 5-(arylsulfonyl), 5-(arylsulfinyl) and 5-(arylsulfanyl)thiazolidine-2,4-diones for inhibition of farnesyl-protein transferase)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 45 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:874965 HCAPLUS Full-text
DOCUMENT NUMBER: 139:364958
TITLE: Preparation of omega-carboxyaryl substituted diphenyl ureas as raf kinase inhibitors
INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 60 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030207872	A1	20031106	US 2002-42226	20020111 <--
PRIORITY APPLN. INFO.:			US 2002-42226	20020111 <--
OTHER SOURCE(S):	MARPAT 139:364958			

AB Urea derivs. of formula A-NHCONH-B or pharmaceutically acceptable salts thereof [A = a substituted moiety of up to 40 carbon atoms of the formula -L-(M-L1)q; where L = a 5 or 6 membered cyclic structure bound directly to D; L1 = a substituted cyclic moiety having at least 5 members; M = a bridging group having at least one atom; q = an integer of 1-3; each cyclic structure of L and L1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur; B = a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur] are prepared These compds. are useful for raf mediated diseases, in particular a cancerous cell growth mediated by raf kinase. All compds. exemplified, e.g. N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4- pyridyloxy]phenyl]urea, displayed IC50 of between 1 mM and 10 μM.

IT 284462-06-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[[2-[N-(2-triisopropylsilyloxyethyl)carbamoyl]-4-pyridyl]oxy]phenyl]urea
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of ω-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)

RN 284462-06-2 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-[[tris(1-methylethyl)silyl]oxy]ethyl]- (CA INDEX NAME)

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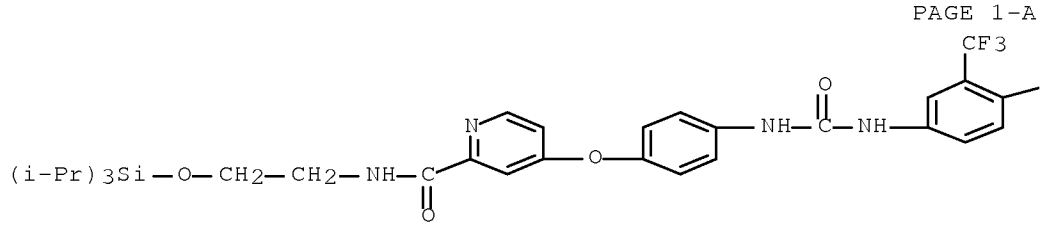

PAGE 1-B

IC ICM C07D417-02
ICS C07D413-02; C07D043-02; C07D041-02; A61K031-541; A61K031-5377; A61K031-496; A61K031-4545; A61K031-454; A61K031-427
INCL 514227800; 514235500; 514252130; 514252140; 514253010; 514254010; 514316000; 514326000; 514365000; 514397000
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 7, 27
IT 349-65-5P, 2-Methoxy-5-(trifluoromethyl)aniline 703-12-8P, N-Methyl-4-bromobenzenesulfonamide 883-62-5P, 3-Methoxy-2-naphthoic Acid 1215-98-1P, 4-(4-Acetylphenoxy)aniline 13041-60-6P, Methyl 3-methoxy-2-naphthoate 16588-75-3P, 2-Methoxy-5-(trifluoromethyl)phenyl isocyanate 27237-21-4P, 4-(3-Carboxyphenoxy)-1-nitrobenzene 36089-89-1P, 4-(4-Methylsulfonylphenoxy)-1-nitrobenzene 41513-02-4P, 4-Bromo-3-(trifluoromethyl)phenyl Isocyanate 50727-06-5P, 5-Hydroxyisoindoline-1,3-dione 51727-15-2P, 4-Chloropyridine-2-carbonyl chloride hydrochloride 53750-66-6P, 4-Chloropyridine-2-carbonyl chloride 54579-63-4P, 4-(3-Carboxyphenoxy)aniline 64064-63-7P, 4-(2-Methyl-5-pyridyloxy)-1-nitrobenzene 67291-63-8P, 2-Amino-3-methoxynaphthalene 71708-64-0P, 4-[3-(N-Methylcarbamoyl)phenoxy]-1-nitrobenzene 73441-73-3P, 4-[4-(N-Methylsulfamoyl)phenoxy]-1-nitrobenzene 73441-86-8P, 4-[4-(N-Methylsulfamoyl)phenyloxy]aniline 75919-92-5P, 4-(4-Acetylphenoxy)-1-nitrobenzene 77992-50-8P, 4-Bromo-3-(trifluoromethyl)aniline monohydrochloride 99586-65-9P, 4-Chloro-2-pyridinecarboxamide 114780-06-2P, 4-Chloro-N,N-dimethyl-2-pyridinecarboxamide 119431-22-0P, 3-Chloro-4-(2,2,2-trifluoroacetylamino)phenol 153435-79-1P, N-Methyl-3-bromobenzenesulfonamide 176977-85-8P, Methyl 4-chloropyridine-2-carboxylate hydrochloride 220000-87-3P, 4-Chloro-N-methyl-2-pyridinecarboxamide 228401-15-8P, 2-[N-(Carbobenzyloxy)amino]-3-methoxynaphthalene 228401-43-2P, 4-(3-Methoxycarbonyl-4-methoxyphenoxy)-1-nitrobenzene 228401-44-3P, 4-(3-Carboxy-4-methoxyphenoxy)-1-nitrobenzene 284461-86-5P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(methoxycarbonyl)-5-pyridyloxy]phenyl]urea 284462-06-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[[2-[N-(2-triisopropylsilyloxyethyl)carbamoyl]-4-pyridyl]oxy]phenyl]urea 284462-37-9P, 4-[2-(N-Methylcarbamyl)-4-pyridyloxy]aniline 284462-38-0P, 5-(4-Nitrophenoxy)isoindoline-1,3-dione 284462-39-1P, 5-(4-Aminophenoxy)isoindoline-1,3-dione 284462-40-4P, 1-(4-tert-Butyl-2-nitrophenyl)-2,5-dimethylpyrrole 284462-41-5P, 5-tert-Butyl-2-(2,5-dimethylpyrrolyl)aniline 284462-42-6P, 4-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-2-methylaniline hydrochloride 284462-43-7P 284462-44-8P, 4-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-2-chloroaniline 284462-45-9P, 4-Chloro-2-methoxy-5-(trifluoromethyl)aniline 284462-46-0P, 4-[3-(N-Methylcarbamoyl)-4-methoxyphenoxy]-1-nitrobenzene 284462-47-1P, 4-[3-(N-Methylcarbamoyl)-4-methoxyphenoxy]aniline 284462-48-2P, 5-(4-Nitrophenoxy)-2-methylisoindoline-1,3-dione 284462-49-3P, 5-(4-Aminophenoxy)-2-methylisoindoline-1,3-dione 284462-51-7P, 4-Chloro-2-[N-(2-morpholin-4-ylethyl)carbamoyl]pyridine 284462-52-8P, 4-[2-[N-(2-Morpholin-4-

ylethyl)carbamoyl]-4-pyridyloxy]aniline 284462-53-9P, 4-(1-Oxoisoindolin-5-yloxy)-1-nitrobenzene 284462-54-0P, 4-(1-Oxoisoindolin-5-yloxy)aniline 284462-55-1P, 4-(3-Ethoxycarbonylphenoxy)-1-nitrobenzene 284462-56-2P, 4-[3-(N-Methylcarbamoyl)phenoxy]aniline 284462-57-3P, 4-(5-Methoxycarbonyl-3-pyridyloxy)-1-nitrobenzene 284462-58-4P, 4-(5-Methoxycarbonyl-3-pyridyloxy)aniline 284462-59-5P, 4-[3-(N-Methylsulfamoyl)phenyloxy]benzene 284462-60-8P, 4-[3-(N-Methylsulfamoyl)phenyloxy]-1-nitrobenzene 284462-61-9P, 4-(3-Methylsulfamoylphenoxy)aniline 284462-62-0P, 4-[4-[1-(Methoxyimino)ethyl]phenoxy]aniline hydrochloride 284462-63-1P, 4-Chloro-N-(2-triisopropylsilyloxy)ethylpyridine-2-carboxamide 284462-64-2P, 4-[[2-[N-(2-Triisopropylsilyloxyethyl)carbamoyl]-4-pyridyl]oxy]aniline 284462-65-3P, 4-(2-Methoxycarbonyl-5-pyridyloxy)-1-nitrobenzene 284462-66-4P, 4-(2-Methoxycarbonyl-5-pyridyloxy)aniline 284462-74-4P, 4-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-2-methylaniline 284462-77-7P, 5-tert-Butyl-2-methoxyphenyl isocyanate 284462-78-8P, 3-[-2-(N-Methylcarbamoyl)-4-pyridyloxy]aniline 284462-79-9P, 3-(2-Carbamoyl-4-pyridyloxy)aniline 284462-80-2P, 4-(2-Carbamoyl-4-pyridyloxy)aniline 284462-82-4P, 4-[2-(N-Ethylcarbamoyl)-4-pyridyloxy]aniline 284462-83-5P, 4-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-3-chloroaniline 284462-84-6P 284462-85-7P, 4-(3-Carbamoylphenoxy)aniline 284462-86-8P, 4-[2-(N,N-Dimethylcarbamoyl)-4-pyridyloxy]aniline 284462-89-1P, 4-[2-(N-Isopropylcarbamoyl)-4-pyridyloxy]aniline 284462-92-6P, 3-[2-(N-Methylcarbamoyl)-4-pyridyloxy]-4-methylaniline 284462-93-7P, 4-[3-[N-(2-Morpholinylethyl)carbamoyl]phenoxy]aniline 284462-94-8P, 4-[3-[N-(2-Piperidylethyl)carbamoyl]phenoxy]aniline 284462-95-9P, 4-[3-[N-(Tetrahydrofurylmethyl)carbamoyl]phenoxy]aniline 284462-99-3P, 4-Chloro-2-methoxy-5-(trifluoromethyl)phenyl isocyanate 284670-99-1P, 4-(4-Acetylphenoxy)-5-aminopyridine 284671-00-7P, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-[4-[3-(5-methoxycarbonylpyridyl)oxy]phenyl]urea 284671-01-8P, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-(3-carboxyphenyl)urea 573673-51-5P, 4-[4-[2-(N-Methylcarbamoyl)phenyl]thio]aniline 573673-52-6P, 3-[4-[2-(N-Methylcarbamoyl)phenyl]thio]aniline 573673-55-9P, 4-[3-[N-[(1-Methyl-2-pyrrolidinyl)methyl]carbamoyl]phenoxy]aniline 604813-03-8P, 4-(5-Methylcarbamoyl-3-pyridyloxy)aniline 604813-05-0P 604813-07-2P, 4-Chloro-N-ethyl-2-pyridinecarboxamide 604813-08-3P, 4-Chloro-N-isopropyl-2-pyridinecarboxamide 604813-09-4P, 4-[4-(N-Methylsulfamoyl)phenoxy]benzene 604813-11-8P, 4-[3-[N-(2-Morpholinylethyl)carbamoyl]phenoxy]-1-nitrobenzene 604813-12-9P, 4-[3-[N-(2-Piperidylethyl)carbamoyl]phenoxy]-1-nitrobenzene 604813-13-0P, 4-[3-[N-(Tetrahydrofurylmethyl)carbamoyl]phenoxy]-1-nitrobenzene 604813-14-1P, 4-[3-[N-[(1-Methyl-2-pyrrolidinyl)methyl]carbamoyl]phenoxy]-1-nitrobenzene

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of ω-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)

IT 228418-48-2P 284461-33-2P 284461-34-3P 284461-35-4P 284461-36-5P
284461-37-6P 284461-38-7P 284461-39-8P 284461-40-1P 284461-41-2P
284461-42-3P 284461-43-4P 284461-44-5P
284461-45-6P 284461-46-7P 284461-47-8P
284461-48-9P 284461-49-0P 284461-50-3P
284461-51-4P 284461-52-5P 284461-53-6P 284461-54-7P
284461-55-8P 284461-56-9P 284461-57-0P 284461-58-1P
284461-59-2P 284461-60-5P 284461-61-6P 284461-62-7P
284461-63-8P 284461-64-9P 284461-65-0P 284461-66-1P 284461-67-2P
284461-68-3P 284461-70-7P 284461-71-8P 284461-72-9P
284461-73-0P 284461-74-1P 284461-75-2P

284461-76-3P 284461-77-4P 284461-78-5P 284461-79-6P
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284461-89-8P 284461-90-1P 284461-91-2P 284461-92-3P
284461-93-4P 284461-94-5P 284461-95-6P 284461-96-7P 284461-97-8P
284461-99-0P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(3-methylcarbamoylphenyl)carbamoylphenyl]urea 284462-00-6P 284462-01-7P
284462-02-8P 284462-03-9P 284462-04-0P 284462-05-1P
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284462-12-0P 284462-13-1P 284462-15-3P 284462-16-4P
284462-17-5P 284462-18-6P 284462-19-7P
284462-20-0P 284462-21-1P 284462-22-2P
284462-23-3P 284462-24-4P 284462-25-5P 284462-26-6P
284462-27-7P 284462-28-8P 284462-29-9P
284462-30-2P 284462-31-3P 284462-34-6P
284462-35-7P, N-[5-(tert-Butyl)-2-(2,5-dimethylpyrrolyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284462-36-8P
284462-70-0P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[N-[3-[N-(3-pyridyl)carbamoyl]phenyl]carbamoyl]phenyl]urea 284670-98-0P,
N,N'-Bis[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 447457-08-1P
573673-43-5P 604813-02-7P 604813-04-9P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[[3-[5-(2-dimethylaminoethyl)carbamoyl]pyridyl]oxy]phenyl]urea 620962-97-2P 620962-98-3P
620962-99-4P 620963-00-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ω-carboxyaryl substituted di-Ph ureas as raf kinase inhibitors for treating raf-mediated diseases such as cancerous cell growth)

L110 ANSWER 46 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:590832 HCAPLUS Full-text
DOCUMENT NUMBER: 139:149528
TITLE: Preparation of diphenylureas as RAF kinase inhibitors
INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 62 pp., Cont. of U. S. Ser. No. 42,203.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20030144278	A1	20030731	US 2002-283248		20021030 <--
US 7235576	B1	20070626	US 2002-42203		20020111 <--
PRIORITY APPLN. INFO.:			US 2001-367380P	P	20010112 <--
			US 2002-42203	A1	20020111 <--

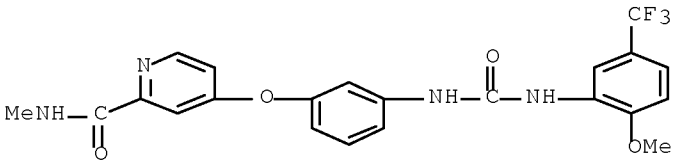
OTHER SOURCE(S): MARPAT 139:149528
AB ADB [I; D = NHCONH; A = L(ML1)q; L = 5-6 membered cyclic structure bound directly to D; L1 = substituted cyclic moiety having ≥5 members, M = bridging group having ≥1 atom; q = 1-3; L, L1 contain 0-4 N, O, S; B = (substituted) up to tricyclic aryl, heteroaryl of ≤30 C atoms with ≥1 6-membered cyclic

structure bound directly to D containing 0-4 N, O, S], were prepared Thus, 4-chloro-3-(trifluoromethyl)phenyl isocyanate in CH2Cl2 was added dropwise to a suspension of 4-[2-(N-methylcarbamoyl)-4-pyridyloxy]aniline (preparation given) in CH2Cl2 at 0°; the resulting mixture was stirred at room temperature for 22 h. to afford N-[4-chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)- 4-pyridyloxy]phenyl]urea. I inhibited RAF kinase in the range 1 nM-1 μM. I pharmaceutical compns. are claimed.

IT 284461-42-3P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diphenylureas as RAF kinase inhibitors)

RN 284461-42-3 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM A61K031-541
ICS A61K031-5377; A61K031-496; A61K031-454; A61K031-4025; C07D417-02; C07D413-02; C07D043-02

INCL 514227800; 514231500; 514252130; 514326000; 514422000; 544060000; 544111000; 544359000; 546207000

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 25, 63

IT 228418-48-2P 284461-33-2P, N-(3-tert-Butylphenyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl urea 284461-34-3P, N-(3-tert-Butylphenyl)-N'-[4-(4-acetylphenoxy)phenyl urea 284461-35-4P 284461-36-5P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl]urea 284461-37-6P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[4-methoxy-3-(N-methylcarbamoy l)phenoxy]phenyl]urea 284461-38-7P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1,3-dioxoisoindolin-5-yloxy)phenyl]urea 284461-39-8P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1-oxoisoindolin-5-yloxy)pheny l] urea 284461-40-1P 284461-41-2P 284461-42-3P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea 284461-43-4P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy) phenyl] urea 284461-44-5P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea 284461-45-6P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy) phenyl] urea 284461-46-7P 284461-47-8P 284461-48-9P 284461-49-0P 284461-50-3P 284461-51-4P 284461-52-5P 284461-53-6P 284461-54-7P, N-[2-Methoxy-5-(trifluoromethyl)phenyl-N'-[4-(1,3-dioxoisoindolin-5-yloxy) phenyl] Urea 284461-55-8P 284461-56-9P 284461-57-0P 284461-58-1P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridylthio]phenyl] urea 284461-59-2P 284461-60-5P 284461-61-6P 284461-62-7P 284461-63-8P 284461-64-9P

284461-65-0P 284461-66-1P 284461-67-2P 284461-68-3P 284461-69-4P
284461-70-7P 284461-71-8P 284461-72-9P 284461-73-0P,
N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridylox y)phenyl]urea 284461-75-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridylox y)phenyl] urea 284461-76-3P,
N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284461-77-4P 284461-78-5P
284461-80-9P 284461-81-0P 284461-82-1P
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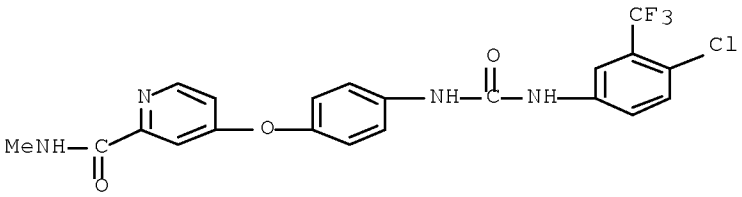
284462-12-0P 284462-13-1P 284462-15-3P 284462-16-4P
284462-17-5P 284462-18-6P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284462-19-7P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[2-chloro-4-[2-(N-methylcarbamoyl)(4-pyridyloxy)]phenyl]urea 284462-20-0P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-chloro-4-[2-(N-methylcarbamoyl)(4-pyridyloxy)]phenyl]urea 284462-21-1P 284462-22-2P,
N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl]urea 284462-23-3P 284462-24-4P
284462-25-5P 284462-26-6P 284462-27-7P 284462-28-8P,
N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[4-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea 284462-29-9P
284462-30-2P 284462-31-3P, N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[3-[2-(N-methylcarbamoyl)-4-pyridyloxy]phenyl] urea 284462-32-4P 284462-34-6P 284462-35-7P
284462-67-5P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(4-aminophenyl) Urea 284462-68-6P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(4-ethoxycarbonylphenyl)urea 284462-70-0P 284462-97-1P 284670-98-0P
447457-08-1P 447457-09-2P 474642-51-8P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(3-carboxyphenyl)urea 474642-55-2P
573673-42-4P 573673-43-5P 573673-45-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diphenylureas as RAF kinase inhibitors)

IT 98-98-6, Picolinic acid 100-51-6, Benzyl alcohol, reactions 106-50-3, p-Phenylenediamine, reactions 108-00-9 109-85-3 110-13-4, Acetonylacetone 110-91-8, Morpholine, reactions 123-30-8, 4-Aminophenol 123-39-7 320-51-4, 4-Chloro-3-trifluoromethylaniline 327-78-6, 4-Chloro-3-trifluoromethylphenyl isocyanate 349-65-5 350-46-9 393-36-2 462-08-8, 3-Pyridinamine 593-56-6, O-Methylhydroxylamine hydrochloride 610-35-5, 4-Hydroxyphthalic acid 619-08-9 626-61-9 883-99-8, Methyl 3-hydroxy-2-naphthoate 1121-78-4 1215-98-1 1664-40-0 1877-71-0 2038-03-1, 4-Morpholineethanamine 2835-99-6, 4-Amino-3-methylphenol 2905-24-0 3535-88-4 5369-19-7 6310-19-6, 2-Nitro-4-tert-butylaniline 6628-77-9 6927-86-2 7781-98-8 16588-75-3 25900-61-2 29264-35-5 30766-22-4 30806-83-8 34803-66-2 36265-31-3 51639-48-6 73441-86-8 150009-83-9 256340-75-7 284461-86-5 284462-06-2 284462-44-8
284462-71-1 284462-72-2 284462-73-3 284462-74-4 284462-76-6
284462-77-7 284462-78-8 284462-79-9 284462-80-2 284462-82-4
284462-84-6 284462-85-7 284462-86-8 284462-89-1 284462-92-6
284462-93-7 284462-94-8 284462-95-9 284462-99-3 284670-99-1

284671-01-8 573673-48-0 573673-49-1 573673-50-4 573673-51-5
573673-52-6 573673-53-7 573673-55-9 573673-56-0
573673-58-2 573673-59-3 573673-60-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of diphenylureas as RAF kinase inhibitors)

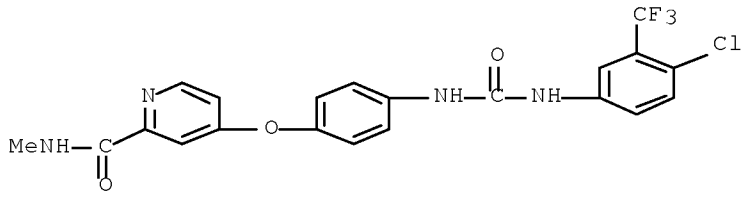
L110 ANSWER 47 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:123969 HCAPLUS Full-text
DOCUMENT NUMBER: 141:166948
TITLE: Raf pathway inhibitors in oncology
AUTHOR(S): Bollag, Gideon; Freeman, Scott; Lyons, John F.; Post, Leonard E.
CORPORATE SOURCE: Plexxikon Inc, Berkeley, CA, 94710, USA
SOURCE: Current Opinion in Investigational Drugs (Thomson Current Drugs) (2003), 4(12), 1436-1441
CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER: Thomson Current Drugs
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Recognition of the importance of the Raf pathway in the proliferation and survival of tumor cells recently increased with the discovery of activating BRAF mutations in human tumors. Therefore, in addition to a role in controlling tumors with Ras mutations and activated growth factor receptors, inhibitors of the Raf pathway may harbor therapeutic potential in tumors carrying a BRAF oncogene. A variety of agents have been discovered that interfere with the Raf pathway, including antisense oligonucleotides and small mols. These inhibitors block the expression of Raf protein, block Ras/Raf interaction, block its kinase activity, or block the kinase activity of the Raf target protein mitogen-activated protein kinase kinase. Raf pathway inhibitors that are currently undergoing clin. evaluation show promising signs of anticancer efficacy with a very tolerable safety profile. Indeed, the Raf inhibitor BAY-43-9006 recently entered phase III clin. trials. Here, we review the current development status of potential Raf pathway therapeutics.
IT 284461-73-0, BAY-43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Raf pathway inhibitors were currently in clin. trial and showed promising anticancer efficacy with very tolerable safety profile and BAY-43-9006 recently entered phase III clin. trial)
RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-0 (Pharmacology)
IT 284461-73-0, BAY-43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(Raf pathway inhibitors were currently in clin. trial and showed promising anticancer efficacy with very tolerable safety profile and BAY-43-9006 recently entered phase III clin. trial)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 48 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:736198 HCAPLUS Full-text
DOCUMENT NUMBER: 139:301125
TITLE: BAY-43-9006(Bayer/Onyx)
AUTHOR(S): Lee, John T.; McCubrey, James A.
CORPORATE SOURCE: Department of Microbiology and Immunology, Brody School of Medicine at East Carolina University, Greenville, NC, 27858-4353, USA
SOURCE: Current Opinion in Investigational Drugs (Thomson Current Drugs) (2003), 4(6), 757-763
CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER: Thomson Current Drugs
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Bayer and Onyx are developing BAY-43-9006, an oral cytostatic Raf kinase inhibitor for the potential treatment of colorectal and breast cancers, hepatocellular carcinoma and non-small-cell lung cancer, in addition to acute myelogenous leukemia, myelodysplastic syndrome and other cancers. A US IND was filed in May 2000 and by Feb. 2003 BAY-43-9006 was in phase II trials, with phase III trials expected to begin later in 2003.
IT 284461-73-0, BAY 43-9006
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAY 43-9006 for treatment of cancer patients)
RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



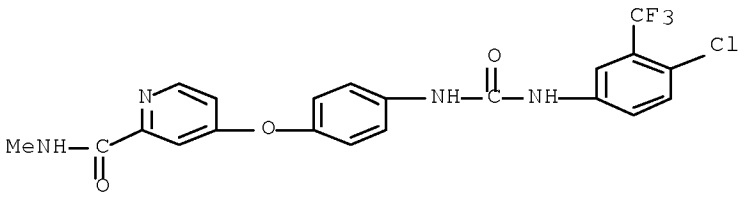
CC 1-0 (Pharmacology)
IT 284461-73-0, BAY 43-9006
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAY 43-9006 for treatment of cancer patients)
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 49 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:12708 HCAPLUS Full-text

DOCUMENT NUMBER: 140:70551
TITLE: A Phase I clinical and pharmacokinetic study of the Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors
AUTHOR(S): Richly, H.; Kupsch, P.; Passage, K.; Grubert, M.; Hilger, R. A.; Kredtke, S.; Voliotis, D.; Scheulen, M. E.; Seeber, S.; Strumberg, D.
CORPORATE SOURCE: West German Cancer Center, University of Essen, Essen, Germany
SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2003), 41(12), 620-621
CODEN: ICTHEK; ISSN: 0946-1965
PUBLISHER: Dustri-Verlag Dr. Karl Feistle
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: The primary objective of this phase I study was to define the safety profile of BAY 43-9006 administered in combination with doxorubicin. Patients and methods: Twenty-nine patients with advanced, refractory solid tumors were treated with doxorubicin (60mg/m2) every 3 wk for 6 consecutive cycles. BAY 43-9006 in combination with doxorubicin chemotherapy was administered at 3 dose levels. Results: Toxicity and response were evaluable in a total of 24 out of 29 enrolled patients. Dose-limiting toxicity was observed at various dose levels. Doxorubicin plasma Cmax/AUC values increased on escalating the dose of BAY 43-9006. Patients with liver metastases and elevated values of AST and conjugated bilirubin, compared to patients with normal hepatic function, showed a higher AUC for doxorubicin at all dose levels. Conclusions: Our data suggest a pharmacol. interaction of BAY 43-9006 at DL 400 mg bid with doxorubicin resulting in significantly increased AUC for doxorubicin.

IT 284461-73-0, BAY 43-9006
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. and pharmacokinetic study of Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors)
RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-6 (Pharmacology)
IT 284461-73-0, BAY 43-9006
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. and pharmacokinetic study of Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors)

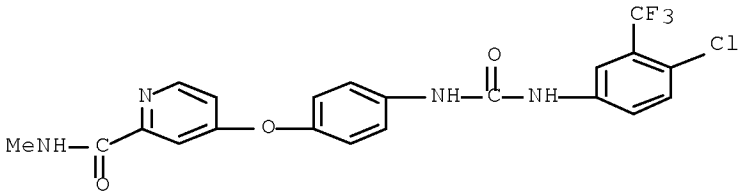
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 50 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:12707 HCAPLUS Full-text
DOCUMENT NUMBER: 140:70550
TITLE: Drug-drug interaction pharmacokinetic study with the Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors
AUTHOR(S): Mross, K.; Steinbild, S.; Baas, F.; Reil, M.; Buss, P.; Mersmann, S.; Voliotis, D.; Schwartz, B.; Brendel, E.
CORPORATE SOURCE: Tumor Biology Center at the Albert-Ludwigs-University Freiburg, Leverkusen, Germany
SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2003), 41(12), 618-619
CODEN: ICTHEK; ISSN: 0946-1965
PUBLISHER: Dustri-Verlag Dr. Karl Feistle
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Classical cytotoxic anticancer drugs generally have specific actions but also interfere with signalling pathways. A logical approach is therefore to combine the Raf kinase inhibitor (RKI) with classical cytotoxic agents since recent work has shown that the RKI BAY 43-9006 and CPT-11 have additive or synergistic actions. Objective: Because a pharmacol. drug-drug interaction cannot be ruled out, interaction studies were started using the RKI BAY 43-9006 in combination with the most important anticancer drugs, such as CPT-11. Patients and methods: The study protocol included three groups of 6 patients with solid tumors given different RKI doses and the same dosage of CPT-11. Blood samples for measurement of CPT-11 and SN-38 were obtained both during and in the absence of RKI treatment. Results: Ests. of toxicity, response and pharmacokinetics during the first RKI dose could be made in a total of 9/18 patients. All symptoms of toxicity were considered to be due to CPT-11 or RKI. The PK evaluation showed no significant differences for CPT-11 and SN-38, with or without RKI. Conclusions: The combination CPT-11 and SN-38 PK is not significantly influenced by the addition of RKI. There is no indication that the PK of RKI are influenced significantly by CPT-11 and SN-38.

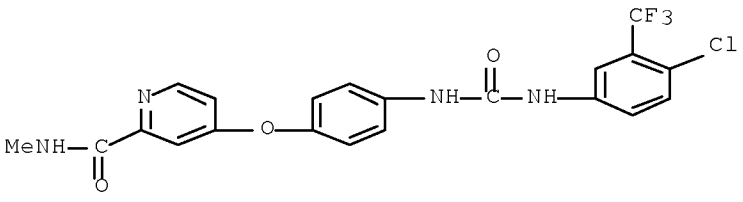
IT 284461-73-0, BAY 43-9006
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug-drug interaction pharmacokinetic study with Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors)

RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



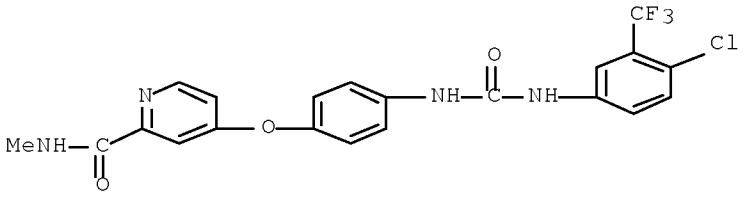
CC 1-6 (Pharmacology)
IT 284461-73-0, BAY 43-9006
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug-drug interaction pharmacokinetic study with Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 51 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:12706 HCAPLUS Full-text
DOCUMENT NUMBER: 141:17009
TITLE: Antitumor effect and potentiation or reduction in cytotoxic drug activity in human colon carcinoma cells by the Raf kinase inhibitor (RKI) BAY 43-9006
AUTHOR(S): Heim, M.; Sharifi, M.; Hilger, R. A.; Scheulen, M. E.; Seeber, S.; Strumberg, D.
CORPORATE SOURCE: West German Cancer Center, University of Essen, Essen, Germany
SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2003), 41(12), 616-617
CODEN: ICTHEK; ISSN: 0946-1965
PUBLISHER: Dustri-Verlag Dr. Karl Feistle
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A study was conducted to evaluate the effects of combining BAY 43-9006 and cytotoxic drugs (paclitaxel, 5-FU, oxaliplatin, and SN-38) on human cancer cells using 4 sequencing protocols and to analyze the effect of RKI on colorectal cancer cells showing marked resistance against SN-38. Results showed the additive action or moderate synergy using RKI in combination with numerous cytotoxic agents and the marked reduction of oxaliplatin activity by RKI in human carcinoma cells. These indicate that Raf kinase activity might be important for oxaliplatin-induced cytotoxicity. Furthermore, lacking cross-resistance between SN-38 and RKI might provide a rationale for designing clin. trials using CPT-11 in combination with BAY 43-9006 in patients with colorectal cancer.
IT 284461-73-0, BAY 43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor effect and potentiation or reduction in cytotoxic drug activity in human colon carcinoma cells by the Raf kinase inhibitor (RKI) BAY 43-9006 in relation to resistance to SN-38)
RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



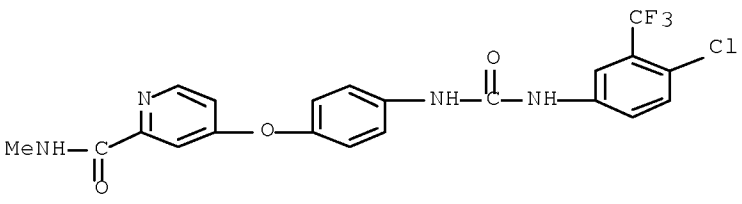
CC 1-6 (Pharmacology)
IT 51-21-8, 5-FU 33069-62-4, Paclitaxel 61825-94-3, Oxaliplatin
86639-52-3, SN-38 284461-73-0, BAY 43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor effect and potentiation or reduction in cytotoxic drug activity in human colon carcinoma cells by the Raf kinase inhibitor (RKI) BAY 43-9006 in relation to resistance to SN-38)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 52 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:12705 HCAPLUS Full-text
DOCUMENT NUMBER: 140:349958
TITLE: Circadian rhythm in the regulation of the MAP kinase pathway - pitfall in the determination of surrogate parameters?
AUTHOR(S): Hilger, R. A.; Diaz-Carballo, D.; Bauer, S.; Kredtke, S.; Scheulen, M. E.; Seeber, S.; Strumberg, D.
CORPORATE SOURCE: Department of Internal Medicine (Cancer Research), West German Cancer Center, University of Essen Medical School, Essen, Germany
SOURCE: International Journal of Clinical Pharmacology and Therapeutics (2003), 41(12), 614-615
CODEN: ICTHEK; ISSN: 0946-1965
PUBLISHER: Dustri-Verlag Dr. Karl Feistle
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A method for the quantification of the inhibitory potency of BAY 43-9006, a novel potent and orally active inhibitor of Raf kinase, measuring the phosphorylated (activated) extracellular signal-regulated kinase (ERK) as a biomarker, was developed. A circadian rhythm in phosphorylation of ERK1/2 proteins after phorbol myristate acetate stimulation was observed It was demonstrated that biomarker measurements could be complicated by circadian variability of the specific mol. target. Phosphorylated ERK1/2 may serve as a biomarker for drugs targeting the mitogen-activated protein kinase cascade. However, the demonstrated circadian regulation demands strict protocols for the realization of biomarker analyses.
IT 284461-73-0, BAY 43-9006
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(circadian rhythm in regulation of MAP kinase pathway)
RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-1 (Pharmacology)
IT 284461-73-0, BAY 43-9006
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(circadian rhythm in regulation of MAP kinase pathway)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 53 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:476541 HCAPLUS Full-text
DOCUMENT NUMBER: 139:143192
TITLE: Activity of the Raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors
AUTHOR(S): DeGrendele, Heather
CORPORATE SOURCE: USA
SOURCE: Clinical Colorectal Cancer (2003), 3(1), 16-18
CODEN: CCCLCF; ISSN: 1533-0028
PUBLISHER: Cancer Information Group
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. BAY 43-9006 is the first orally active Raf kinase inhibitor to undergo clin. testing and has shown promise in the treatment of colorectal cancer. Treatment with BAY 43-9006 has resulted in stable disease in 37 % of patients across this phase I series, with 42 % of colorectal cancer patients achieving stable disease. Among patients achieving stable disease, 27 have been on therapy for over 6 mo without progression. Toxicity associated with this regimen is mild, with few grade 3/4 adverse events reported. Furthermore, fluorescence-activated cell sorter (FACS) anal. demonstrated that treatment with BAY 43-9006 could result in the inhibition of extracellular signal-regulated kinase (ERK) activation. Based on this phase I data, 2 phase II trials, including one in patients with colorectal cancer, have been initiated, and phase III trials are planned for 2003. At the 38th Annual Meeting of the American Society of Clin. Oncol., Vincent and colleagues reported on preclin. studies combining BAY 43-9006 with irinotecan, vinorelbine, or gemcitabine in human xenografts models. They demonstrated that BAY 43-9006 combined with cytotoxic or cytostatic agents is at least as efficacious as the individual agents administered alone. With this as rationale, multiple phase I/II studies are being designed to investigate the role of BAY 43-9006 in combination with standard chemotherapy.
IT 284461-73-0, BAY 43-9006
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(activity of Raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors)
RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-0 (Pharmacology)
IT 284461-73-0, BAY 43-9006
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(activity of Raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 54 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:615574 HCAPLUS Full-text
DOCUMENT NUMBER: 137:169425
TITLE: Preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors
INVENTOR(S): Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Sibley, Robert N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062763	A2	20020815	WO 2002-US3361	20020207 <--
WO 2002062763	A3	20021010		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2002238042	A1	20020819	AU 2002-238042	20020207 <--
AU 2004200722	A1	20040318	AU 2004-200722	20040224 <--
AU 2004200722	B2	20080110		

PRIORITY APPLN. INFO.:	US 2001-777920	A	20010207 <--
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	US 1999-257266	B2	19990225 <--
	US 1999-425228	B2	19991022 <--
	AU 2000-25016	A3	20000112 <--
	US 2001-758548	A2	20010112 <--
	WO 2002-US3361	W	20020207 <--

OTHER SOURCE(S): MARPAT 137:169425
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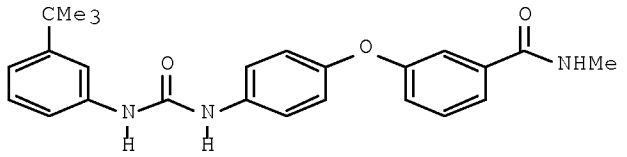


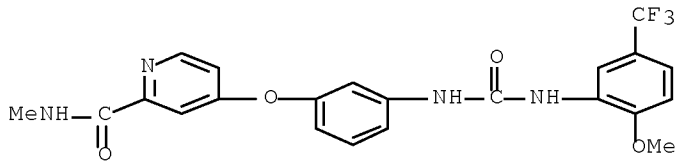
II

AB Title compds., e.g., RNHCONHZOR1 [I; R = C6H4(CMe3)-3, 2-methoxy-5-trifluoromethylphenyl, 4-chloro-3-trifluoromethylphenyl, 2-methoxy-3-quinolyl, etc.; R1 = (un)substituted acylphenyl, -acylpyridinyl, etc.; Z = (un)substituted 1,3- or -1,4-phenylene] were prepared Thus, 4-(H2N)C6H4OC6H4(CONHMe)-4 (preparation given) was condensed with 3-(Me3C)C6H4NH2 and CO(OCCl3)2 to give title compound II. Data for biol. activity of title compds. were given.

IT 284461-42-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)

RN 284461-42-3 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[[2-methoxy-5-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D215-38
ICS C07D401-12; A61K031-4406; A61K031-47; A61P035-00; C07D401-12; C07D215-00; C07D213-00; C07D401-12; C07D215-00; C07D209-00

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

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447457-09-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-aryl-N'-[(acylphenoxy)phenyl]ureas as raf kinase inhibitors)

L110 ANSWER 55 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:314913 HCAPLUS Full-text
DOCUMENT NUMBER: 136:340689
TITLE: Preparation of urea derivatives containing nitrogenous aromatic ring compounds as inhibitors of angiogenesis
INVENTOR(S): Funahashi, Yasuhiro; Tsuruoka, Akihiko; Matsukura, Masayuki; Haneda, Toru; Fukuda, Yoshio; Kamata, Junichi; Takahashi, Keiko; Matsushima, Tomohiro; Miyazaki, Kazuki; Nomoto, Kenichi; Watanabe, Tatsuo; Obaishi, Hiroshi; Yamaguchi, Atsumi; Suzuki, Sachi; Nakamura, Katsuji; Mimura, Fusayo; Yamamoto, Yuji; Matsui, Junji; Matsui, Kenji; Yoshiba, Takako; Suzuki, Yasuyuki; Arimoto, Itaru
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 699 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032872	A1	20020425	WO 2001-JP9221	20011019 <--
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OTHER SOURCE(S): MARPAT 136:340689

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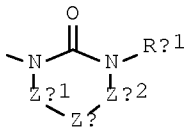
Q= 

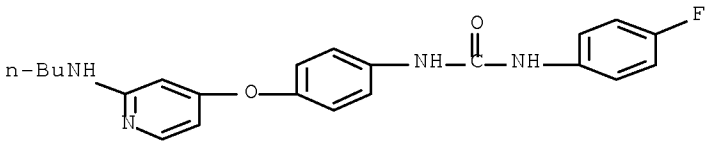
AB N-aryl or N-heteroarylurea derivs. represented by the general formula Ag-Xg-Yg-Tg1 or salts thereof, or hydrates of both [wherein Ag = (un)substituted C6-14 aryl or 5- to 14-membered heterocyclic group; Xg = single bond, O, S, C1-6 alkylene, SO, SO2, (un)substituted NH; Yg = (un)substituted C6-14 aryl, 5- to 14-membered heterocyclic group, C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14

aryl-C1-6 alkyl, 5- to 14-membered heteroaryl-C1-6 alkyl, (CH2)gSO2 (g = 1-8), (CH2)faCH:CH(CH2)fb (fa, fb = 0, 1,2,3), etc.; and Tg1 = a group of the general formula -Eg-CO-NRg1(Zg) or Q; wherein Eg = a single bond, (un)substituted NH; Rg1 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 aliphatic hydrocarbyl, etc.; Zg = C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl, etc.; Zg1, Zg2 = (a) a single bond, (b) C1-6 alkylene optionally having ≥1 atoms selected from O, S, and N in the middle or the terminus of the chain and optionally substituted with oxo, (c) (un)substituted C2-6 alkenyl] are prepared These compds. are also inhibitors of vascular endothelial growth factor receptor kinase (VEGFR2 kinase) and are useful as antitumor agents against hemangioma, pancreatic cancer, stomach cancer, colon cancer, breast cancer, prostate cancer, lung cancer, brain tumor, leukemia, or ovarian cancer, as cancer metastasis inhibitors, and for the treatment of retina neovascularization, diabetic retinopathy, atherosclerosis, or inflammatory diseases such as osteoarthritis, rheumatoid arthritis, psoriasis, or delayed hypersensitivity. Thus, to solution of 334 mg 4-[6-(4-benzyloxyphenyl)-7-(2- trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2- chlorophenylamine in 4 mL DMF were added 0.066 mL pyridine and 0.102 mL Ph chlorocarbonate and stirred at room temperature for 2.5 h to give 330 mg N-[4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea which (260 mg) was hydrogenolyzed over platinum oxide in ethanol overnight to give 160 mg N-[4-[6-(4-hydroxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H- pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea (I). I showed IC50 of 0.02 nM for inhibiting the vascular endothelial growth factor (VEGF)-stimulated sandwich tube formation in vascular endothelial cell.

IT 417714-74-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of urea derivs. containing nitrogenous aromatic ring compds. as
angiogenesis inhibitors for prevention or treatment of diseases)

RN 417714-74-0 HCAPLUS

CN Urea, N-[4-[[2-(butylamino)-4-pyridinyl]oxy]phenyl]-N'-(4-fluorophenyl)- (CA INDEX NAME)



IC ICM C07D213-74
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CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 27

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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of urea derivs. containing nitrogenous aromatic ring compds. as

angiogenesis inhibitors for prevention or treatment of diseases)

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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of urea derivs. containing nitrogenous aromatic ring compds. as
angiogenesis inhibitors for prevention or treatment of diseases)

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417723-37-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of urea derivs. containing nitrogenous aromatic ring compds. as
angiogenesis inhibitors for prevention or treatment of diseases)

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417724-74-4P, 4-(4-Aminophenoxy)pyrimidine 417724-75-5P,
N-(4-(7-Benzyloxy-6-cyano-4-quinolyloxy)phenyl)-N'-(4-fluorophenyl)urea
417724-80-2P, N-(3-(6,7-Dimethoxy-4-quinolinyloxy)propyl)phthalimide
417724-81-3P 417724-86-8P, N-Cyclopropyl-5-[(2-(2-chloroacetylamino)-4-
pyridyl)oxy]-1H-1-indolecarboxamide 417724-87-9P, N-Cyclopropyl-5-[(2-
((3-bromopropionyl)amino)-4-pyridyl)oxy]-1H-1-indolecarboxamide
417724-88-0P, 4-[2-[(4-[3-Chloro-4-[(phenoxycarbonyl)amino]phenoxy]-2-
pyridyl)amino]-2-oxoethyl]-1-piperidinecarboxylic acid tert-butyl ester
417724-89-1P, N-Phenyl-3-chloro-5-[(2-[[(4-piperidyl)carbonyl]amino]-4-
pyridyl)oxy]-1H-1-indolecarboxamide 417724-90-4P, 2-[(4-
Chlorobutyryl)amino]-4-(4-nitrophenoxy)pyridine 417724-91-5P
417724-92-6P, 4-(2-Chloro-6-[(diphenylmethylene)amino]pyridin-3-yloxy)-6,7-
dimethoxyquinoline 417724-94-8P, (4-(4-Nitrophenoxy)-7-methoxyquinolin-6-
yl)carbamic acid benzyl ester 417724-95-9P,
7-(((2R)-2-(Triethylsilyloxy)-3-(pyrrolidin-1-yl)propyl)oxy)-4-(1H-indol-5-
yloxy)quinoline-6-carbonitrile 417724-96-0P, N-(2-Fluoroethyl)-5-(6-
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yloxy)indole-1-carboxamide 417724-98-2P, 4-(3-Chloro-4-
(((cyclopropylamino)carbonyl)amino)phenoxy)-7-((4-piperidyl)methoxy)-6-
quinolinecarboxamide 417724-99-3P, N-(4-(6-Cyano-7-hydroxy-4-
quinolinyloxy)-2-chlorophenyl)-N'-cyclopropylurea 417725-00-9P,
4-(4-Amino-3-chlorophenoxy)-6-cyano-7-hydroxyquinoline 417725-01-0P,
2-Amino-4-(4-aminophenoxy)-3-aminopyridine 417725-02-1P,
4-(4-Nitrophenoxy)-6-(4-(pyrrolidin-1-yl)phenyl)-7H-pyrrolo[2,3-
d]pyrimidine 417725-05-4P, N'-(4-Benzyloxy-2-methylphenyl)-N-(4-
fluorophenyl)urea 417725-08-7P, 6-Cyano-4-(3-fluoro-4-nitrophenoxy)-7-
hydroxyquinoline 417725-09-8P, 2-Amino-4-(4-nitrophenoxy)-3-
nitropyridine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of urea derivs. containing nitrogenous aromatic ring compds.
as
angiogenesis inhibitors for prevention or treatment of diseases)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 56 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:850357 HCAPLUS Full-text
DOCUMENT NUMBER: 137:352907
TITLE: Preparation of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf kinase for the treatment of tumors and/or cancerous cell growth
INVENTOR(S): Dumas, Jacques; Riedl, Bernd; Khire, Uday; Wood, Jill E.; Robert, Sibley N.; Monahan, Mary-Katherine; Renick, Joel; Gunn, David E.; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 63 pp., Cont.-in-part of U.S. Ser. No. 758,548.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020165394	A1	20021107	US 2001-777920	20010207 <--

CA 2549558	A1	20000720	CA 2000-2549558	20000112 <--
CN 1721397	A	20060118	CN 2005-10089504	20000112 <--
EP 1690853	A1	20060816	EP 2005-28442	20000112 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
ZA 2001005751	A	20030714	ZA 2001-5751	20010712 <--
US 20020137774	A1	20020926	US 2001-907970	20010719 <--
WO 2002062763	A2	20020815	WO 2002-US3361	20020207 <--
WO 2002062763	A3	20021010		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002238042	A1	20020819	AU 2002-238042	20020207 <--
US 20030139605	A1	20030724	US 2002-71248	20020211 <--
AU 2004200722	A1	20040318	AU 2004-200722	20040224 <--
AU 2004200722	B2	20080110		
JP 2006328075	A	20061207	JP 2006-190034	20060711 <--
US 20080032979	A1	20080207	US 2007-845595	20070827 <--

PRIORITY APPLN. INFO.:	US 1999-115877P	P	19990113 <--
	US 1999-257266	B2	19990225 <--
	US 1999-425228	B2	19991022 <--
	US 2001-758548	A2	20010112 <--
	US 1999-115878P	P	19990113 <--
	AU 2000-25016	A3	20000112 <--
	CA 2000-2359510	A3	20000112 <--
	CN 2000-802685	A3	20000112 <--
	EP 2000-903239	A3	20000112 <--
	JP 2000-593580	A3	20000112 <--
	US 2001-777920	A	20010207 <--
	US 2001-948915	A1	20010910 <--
	WO 2002-US3361	W	20020207 <--

OTHER SOURCE(S): MARPAT 137:352907

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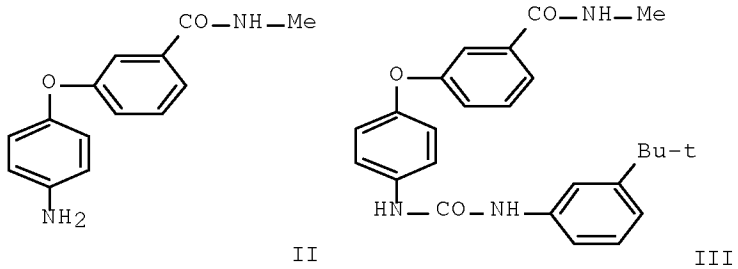


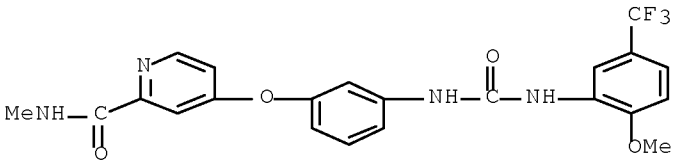
AB Title compds. B-NHCONH-L-(M-L1)q (I) [B = (un)substituted pyridyl, quinolinyl, isoquinolinyl; L = 5 or 6 membered cyclic structure; L1 = substituted cyclic moiety having at least 5 members; M = bridging group having at least one atom; q = 1-3; with proviso that L and L1 contain 0-4 hetero atoms, e.g., N, O and

S] and their pharmaceutically acceptable salts were prepared For example, coupling of aniline II, e.g., prepared from Et 3-hydroxybenzoate in 4-steps, with bis(trichloromethyl)carbonate followed by 3-tert-butylaniline afforded urea III. In in vitro raf kinase assays, 112-specific examples of compds. I inhibited kinase activity with IC50 values ranging from 10 nM-10 μM. Compds. I are useful for the treatment of cancerous cell growth mediated by raf kinase.

IT 284461-42-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf kinase)

RN 284461-42-3 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[[2-methoxy-5-(trifluoromethyl)phenyl]amino] carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



IC ICM C07D217-22
ICS C07D215-38

INCL 546143000

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT 228418-48-2P 284461-33-2P 284461-34-3P 284461-35-4P 284461-36-5P
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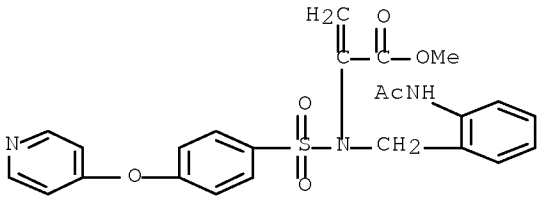
284670-98-0P 432050-20-9P, N-(4-tert-Butylpyridyl)-N'-(4-(4-

chlorophenoxy)phenyl) Urea 432050-22-1P 432050-23-2P 432050-24-3P 432050-25-4P 432050-26-5P 432050-27-6P 432050-28-7P 432050-52-7P 447457-08-1P 447457-09-2P 474642-44-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinolyl, isoquinolyl or pyridyl-ureas as inhibitors of raf kinase)

L110 ANSWER 57 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:732413 HCAPLUS Full-text
DOCUMENT NUMBER: 138:362126
TITLE: Benzodiazepine inhibitors of the MMPs and TACE
AUTHOR(S): Nelson, Frances C.; Delos Santos, Efren; Levin, Jeremy I.; Chen, James M.; Skotnicki, Jerauld S.; DiJoseph, John F.; Sharr, Michele A.; Sung, Amy; Killar, Loran M.; Cowling, Rebecca; Jin, Guixian; Roth, Catherine E.; Albright, J. Donald
CORPORATE SOURCE: Wyeth Research, Pearl River, NY, 10965, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(20), 2867-2870
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:362126
AB A series of benzodiazepine inhibitors of the MMPs and TACE has been developed. These compds. display an interesting selectivity profile and should be useful tools for exploring the biol. relevance of such selectivity.
IT 522623-58-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(benzodiazepine inhibitors of MMPs and TACE)
RN 522623-58-1 HCAPLUS
CN 2-Propenoic acid, 2-[[[2-(acetylamino)phenyl]methyl][[4-(4-pyridinyloxy)phenyl]sulfonyl]amino]-, methyl ester (CA INDEX NAME)



CC 1-3 (Pharmacology)
IT 85622-74-8P 232950-28-6P 233754-49-9P 233754-50-2P 233754-53-5P 233754-54-6P 233754-61-5P 233754-64-8P 233754-67-1P 233754-68-2P 233754-69-3P 233754-71-7P 233754-73-9P 233754-75-1P 233754-80-8P 233754-83-1P 233754-86-4P 233754-87-5P 233754-88-6P 233754-90-0P 233754-91-1P 233754-93-3P 233754-96-6P 233754-99-9P 233755-06-1P 233755-35-6P 233755-36-7P 233755-41-4P 233755-56-1P 233755-57-2P 233755-59-4P 233755-60-7P 233755-61-8P 233755-62-9P 233755-63-0P 233755-71-0P 233755-72-1P 233755-73-2P 233755-75-4P 287121-33-9P 522623-54-7P 522623-55-8P 522623-56-9P 522623-57-0P

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522623-61-6P 522623-62-7P 522623-63-8P 522623-64-9P
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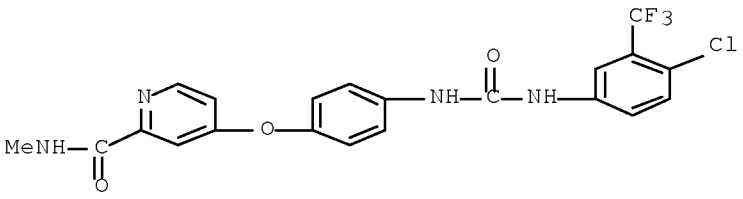
522623-87-6P 597564-87-9P 612491-93-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(benzodiazepine inhibitors of MMPs and TACE)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 58 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:785445 HCAPLUS Full-text
DOCUMENT NUMBER: 138:296904
TITLE: BAY 43-9006: Preclinical data
AUTHOR(S): Wilhelm, Scott; Chien, Du-Shieng
CORPORATE SOURCE: Bayer Research Center, Institute for Preclinical Drug Development, Pharmaceutical Division, Bayer Corporation, West Haven, CT, 06516, USA
SOURCE: Current Pharmaceutical Design (2002), 8(25), 2255-2257
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The drug design and discovery efforts described in the previous section led to the development of a novel, small mol. Raf-1 kinase inhibitor, BAY 43-9006, which belongs to a class that can be broadly described as bis-aryl ureas. BAY 43-9006 was identified during a large medicinal chemical optimization program, and this compound was selected for further pharmacol. characterization based on its potent inhibition of Raf-1 (IC50 12 nM) and its favorable kinase selectivity profile [2, 3]. In vitro and in vivo expts. were designed to demonstrate effective blockade of the Raf/MEK/ERK signaling pathway in tumor cells and for antitumor efficacy in human xenograft models.
IT 284461-73-0, BAY 43-9006
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor BAY 43-9006)
RN 284461-73-0 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-0 (Pharmacology)
IT 284461-73-0, BAY 43-9006
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor BAY 43-9006)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 59 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:785444 HCAPLUS Full-text
DOCUMENT NUMBER: 137:362317
TITLE: BAY 43-9006: Early clinical data in patients with advanced solid malignancies
AUTHOR(S): Hotte, Sebastien J.; Hirte, Hal W.
CORPORATE SOURCE: Department of Medicine, Hamilton Regional Cancer Centre, McMaster University and Division of Medical Oncology, Hamilton, ON, Can.
SOURCE: Current Pharmaceutical Design (2002), 8(25), 2249-2253
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Various signaling pathways can confer the malignant phenotype to a cell. Ras signaling proteins have been found to play an important role in controlling cellular growth. Raf-1 is a protein kinase that exerts its effects downstream of Ras in the mitogen-activated protein kinase pathway and is thus likely to be crucial in the development of the malignant phenotype. BAY 43-9006 is an orally administered selective inhibitor of Raf-1 and the first compound of its class to enter clin. trials. This article describes the early clin. data of BAY 43-9006 in patients with advanced, refractory solid tumors. To date, over 60 patients have been treated as part of four Phase I clin. trials. Dose levels have ranged from 50mg once weekly to 200mg twice-daily in continuous administration. The drug has been generally well tolerated with no dose limiting toxicity yet encountered. The more common toxicities have involved the gastrointestinal tract (diarrhea, nausea, abdominal cramping) and the skin (pruritus, rash, cheilitis). Pharmacokinetic evaluations have found BAY 43-9006 to have considerable interpatient variability. However, there seems to be an increase in Cmax and AUC values with increasing dose. There is no clear effect of food on bioavailability. Splitting the dose to twice-daily administration has shown increases in Cmax and AUC values but is also accompanied by considerable interpatient variability.
IT 475207-59-1, BAY 43-9006 mono-p-tosylate
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAY 43-9006 for patients with advanced solid neoplasm)
RN 475207-59-1 HCAPLUS
CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl-, 4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

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CRN 284461-73-0
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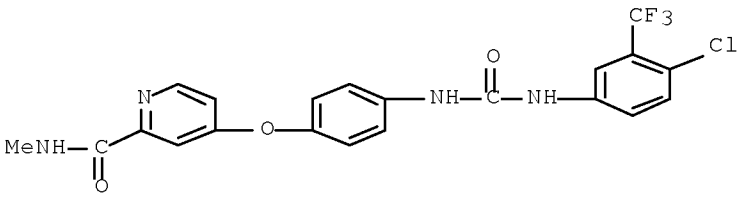

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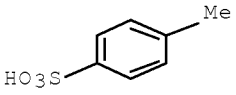


CC 1-0 (Pharmacology)
IT 475207-59-1, BAY 43-9006 mono-p-tosylate
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAY 43-9006 for patients with advanced solid neoplasm)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

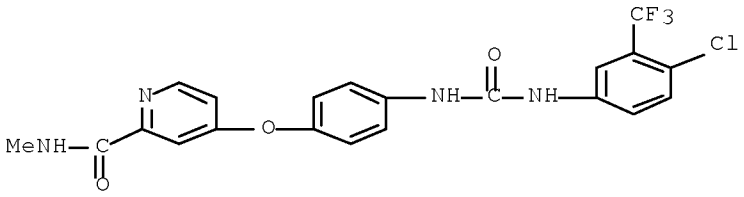
L110 ANSWER 60 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:208292 HCAPLUS Full-text
DOCUMENT NUMBER: 139:269975
TITLE: Oncolytic Raf kinase inhibitor
AUTHOR(S): Sorbera, L. A.; Castaner, J.; Bozzo, J.; Leeson, P. A.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (2002), 27(12), 1141-1147
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with refs. The Ras/Raf/MEK pathway is a signaling module that controls cell growth and survival. Activation of this pathway results in a cascade of events from the cell surface to the nucleus ultimately affecting cellular proliferation, apoptosis, differentiation and transformation. Raf is a serine/threonine kinase that is a downstream effector enzyme of Ras. When activated, Raf goes on to activate MEK1 and MEK2 kinases which in turn phosphorylate and activate ERK1 and ERK2 which translocate to the nucleus where they stimulate pathways required for translation initiation and transcription activation leading to proliferation. Raf kinase has been validated as a potential and attractive target for hyperproliferative disorders such as cancer. Research has recently focused on efforts to discover potent Raf kinase inhibitors and several low-mol.-weight Raf kinase inhibitors have been described. Bis-aryl ureas were identified within this program using

medicinal chemical-directed syntheses or combinatorial libraries. After high-throughput screening of more than 200,000 compds. against recombinant Raf-1 kinase, the orally active Bay-43-9006 was identified as having potent inhibitory activity and was chosen for further development as a treatment for cancer. Bay-43-9006 has exhibited potent in vitro activity against several tumor cell lines and has displayed efficacy in human tumor xenograft models. Moreover, results from phase I development in patients with a variety of cancer types indicates promising clin. efficacy for the compound

IT 284461-73-0, Bay-43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oncolytic Raf kinase inhibitor)

RN 284461-73-0 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



CC 1-0 (Pharmacology)

IT 139691-76-2, Raf kinase 284461-73-0, Bay-43-9006
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oncolytic Raf kinase inhibitor)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 61 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:493516 HCAPLUS Full-text
DOCUMENT NUMBER: 133:120157
TITLE: Preparation of ω-carboxy(hetero)aryl substituted diphenyl ureas as raf kinase inhibitors
INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042012	A1	20000720	WO 2000-US648	20000112 <--

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KR 2001-708847	A3	20010712 <--
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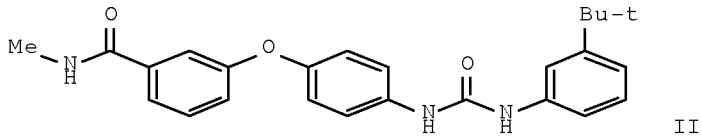
OTHER SOURCE(S): MARPAT 133:120157

GI



II

AB This invention relates to the preparation and use of (hetero)aryl ureas ANHCONHB [I; A = L(ML1)q; L = 5- or 6-membered (hetero)aryl, especially Ph or pyridinyl; M = bridging group; L1 = (hetero)aryl with at least one (un)substituted sulfamoyl, carboxy, or carbamoyl substituent; q = 1-3; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] for the treatment of raf mediated diseases, such as cancer (no data). Approx. 100 invention compds. and numerous intermediates were prepared For instance, 3-tert-butylaniline was coupled with bis(trichloromethyl)carbonate to form the isocyanate, followed by addition of 4-(3-N-methylcarbamoylphenoxy)aniline (preparation given) to afford the urea II.

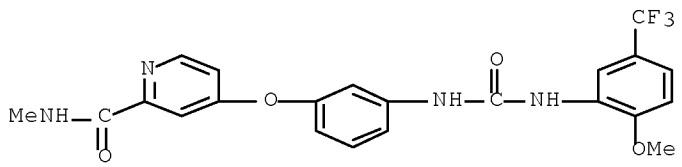
IT 284461-42-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of ω-carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

RN 284461-42-3 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[3-[[[[2-methoxy-5-(trifluoromethyl)phenyl]amino] carbonyl]amino]phenoxy]-N-methyl- (CA INDEX NAME)



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CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1
IT 284461-33-2P, N-(3-tert-Butylphenyl)-N'-(4-(3-(N-methylcarbamoyl)phenoxy)phenyl)urea 284461-34-3P, N-(3-tert-Butylphenyl)-N'-(4-(4-acetylphenoxy)phenyl)urea 284461-36-5P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[3-(N-methylcarbamoyl)phenoxy]phenyl]urea 284461-37-6P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-[4-methoxy-3-(N-methylcarbamoyl)phenoxy]phenyl]urea 284461-39-8P, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1-oxoisoindolin-5-yloxy)phenyl]urea 284461-42-3P 284461-43-4P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea 284461-44-5P 284461-45-6P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl]urea 284461-51-4P 284461-54-7P 284461-58-1P, N-[2-Methoxy-5-(trifluoromethyl)phenyl]-N'-[4-[[2-(N-methylcarbamoyl)-4-pyridyl]thio]phenyl]urea 284461-74-1P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[4-(2-carbamoyl-4-pyridyloxy)phenyl]urea 284461-75-2P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-[3-(2-carbamoyl-4-pyridyloxy)phenyl]urea 284461-78-5P 284461-86-5P 284461-90-1P 284461-99-0P 284462-05-1P 284462-06-2P 284462-17-5P 284462-18-6P 284462-19-7P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[2-chloro-4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea 284462-20-0P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-chloro-4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea 284462-22-2P, N-[4-Bromo-3-(trifluoromethyl)phenyl]-N'-[3-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea 284462-26-6P 284462-28-8P, N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[4-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea 284462-30-2P 284462-31-3P, N-[2-Methoxy-4-chloro-5-(trifluoromethyl)phenyl]-N'-[3-[[2-(N-methylcarbamoyl)-4-pyridyl]oxy]phenyl]urea 284462-35-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of ω-carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)
IT 228418-48-2P 284461-35-4P 284461-40-1P 284461-41-2P 284461-46-7P 284461-47-8P 284461-49-0P 284461-50-3P 284461-52-5P 284461-53-6P 284461-55-8P 284461-56-9P 284461-57-0P 284461-59-2P 284461-60-5P 284461-61-6P 284461-62-7P 284461-63-8P 284461-64-9P 284461-65-0P 284461-66-1P 284461-67-2P 284461-68-3P 284461-69-4P 284461-70-7P 284461-71-8P 284461-72-9P 284461-77-4P 284461-79-6P 284461-80-9P 284461-81-0P 284461-82-1P 284461-83-2P 284461-84-3P 284461-85-4P 284461-88-7P 284461-91-2P 284461-92-3P 284461-93-4P 284461-94-5P 284461-95-6P 284461-96-7P 284461-97-8P 284461-98-9P 284462-00-6P 284462-01-7P 284462-02-8P 284462-03-9P 284462-04-0P 284462-07-3P 284462-08-4P 284462-09-5P 284462-10-8P 284462-11-9P 284462-12-0P 284462-13-1P 284462-15-3P 284462-16-4P 284462-21-1P 284462-23-3P 284462-24-4P 284462-25-5P 284462-27-7P 284462-32-4P 284462-33-5P 284462-34-6P 284462-36-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of ω-carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

IT 98-98-6, Picolinic acid 99-98-9, 4-(Dimethylamino)aniline 106-50-3, p-Phenylenediamine, reactions 108-00-9, N,N-Dimethylethylenediamine 109-85-3, 2-Methoxyethylamine 110-13-4, Acetonylacetone 123-30-8, 4-Aminophenol 320-51-4, 4-Chloro-3-(trifluoromethyl)aniline 327-78-6, 4-Chloro-3-(trifluoromethyl)phenyl isocyanate 349-65-5, 2-Methoxy-5-(trifluoromethyl)aniline 350-46-9, 1-Fluoro-4-nitrobenzene 371-40-4, 4-Fluoroaniline 393-36-2, 4-Bromo-3-(trifluoromethyl)aniline 462-08-8, 3-Aminopyridine 610-35-5, 4-Hydroxyphthalic acid 619-08-9, 2-Chloro-4-nitrophenol 626-61-9, 4-Chloropyridine 883-99-8, Methyl 3-hydroxy-2-naphthoate 1121-78-4, 5-Hydroxy-2-methylpyridine 1215-98-1, 4-(4-Acetylphenoxy)aniline 1664-40-0, N-Phenylethylenediamine 1877-71-0, Monomethyl isophthalate 2038-03-1, 4-(2-Aminoethyl)morpholine 2252-63-3, N-(4-Fluorophenyl)piperazine 2524-67-6, 4-Morpholinoaniline 2835-99-6, 4-Amino-3-methylphenol 2905-24-0, 3-Bromobenzenesulfonyl chloride 5369-19-7, 3-tert-Butylaniline 6310-19-6, 2-Nitro-4-tert-butylaniline 6628-77-9, 5-Amino-2-methoxypyridine 6927-86-2, 4-(4-Acetylphenoxy)aniline hydrochloride 7781-98-8, Ethyl 3-hydroxybenzoate 13154-24-0, Triisopropylsilyl chloride 16588-75-3 25900-61-2, 3-(Methylcarbamoyl)aniline 29264-35-5, 4-(3-Carboxy-4-hydroxyphenoxy)-1-nitrobenzene 30766-22-4, Methyl 5-hydroxynicotinate 30806-83-8, Ethyl 4-isocyanatobenzoate 34803-66-2, N-(2-Pyridyl)piperazine 36265-31-3, 4-(4-Methylthiophenoxy)-1-nitrobenzene 51639-48-6, N-(4-Acetylphenyl)piperazine 73441-86-8 150009-83-9, 3-Amino-2-methoxyquinoline 284461-38-7, N-(5-tert-Butyl-2-methoxyphenyl)-N'-[4-(1,3-dioxoisoindolin-5-yloxy)phenyl]urea 284461-48-9 284461-76-3, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'-(3-((2-(N-Methylcarbamoyl)-4-pyridyl)oxy)phenyl)urea 284462-29-9 284462-72-2, 3-Chloro-6-(N-acetylamino)-4-(trifluoromethyl)anisole 284462-73-3, 4-Chloro-N-(2-hydroxyethyl)pyridine-2-carboxamide 284462-74-4 284462-76-6 284462-77-7, 5-tert-Butyl-2-methoxyphenyl isocyanate 284462-78-8, 3-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]aniline 284462-79-9, 3-(2-Carbamoyl-4-pyridyloxy)aniline 284462-80-2, 4-(2-Carbamoyl-4-pyridyloxy)aniline 284462-82-4, 4-[[2-(N-Ethylcarbamoyl)-4-pyridyl]oxy]aniline 284462-83-5, 4-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]-3-chloroaniline 284462-85-7, 4-(3-Carbamoylphenoxy)aniline 284462-86-8, 4-[[2-(N,N-Dimethylcarbamoyl)-4-pyridyl]oxy]aniline 284462-87-9 284462-88-0 284462-89-1, 4-[[2-(N-Isopropylcarbamoyl)-4-pyridyl]oxy]aniline 284462-92-6, 3-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]-4-methylaniline 284462-93-7, 4-[3-[N-(2-Morpholinylethyl)carbamoyl]phenoxy]aniline 284462-94-8, 4-[3-[N-(2-Piperidylethyl)carbamoyl]phenoxy]aniline 284462-95-9, 4-[3-[N-(Tetrahydrofurylmethyl)carbamoyl]phenoxy]aniline 284462-96-0 284462-99-3, 4-Chloro-2-methoxy-5-(trifluoromethyl)phenyl isocyanate 284670-99-1, 4-(4-Acetylphenoxy)-5-aminopyridine 284671-00-7, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-[4-[3-(5-methoxycarbonylpyridyl)oxy]phenyl]urea 284671-01-8, N-[5-(Trifluoromethyl)-2-methoxyphenyl]-N'-(3-carboxyphenyl)urea
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of ω-carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

IT 883-62-5P, 3-Methoxy-2-naphthoic acid 13041-60-6P, Methyl 3-methoxy-2-naphthoate 27237-21-4P, 4-(3-Carboxyphenoxy)-1-nitrobenzene 36089-89-1P, 4-(4-Methylsulfonylphenoxy)-1-nitrobenzene 41513-02-4P, 4-Bromo-3-(trifluoromethyl)phenyl isocyanate 50727-06-5P, 5-Hydroxyisoindoline-1,3-dione 51727-15-2P, 4-Chloropyridine-2-carbonyl chloride hydrochloride 54579-63-4P, 4-(3-Carboxyphenoxy)aniline

64064-63-7P, 4-[(2-Methylpyridin-5-yl)oxy]-1-nitrobenzene 67291-63-8P, 2-Amino-3-methoxynaphthalene 71708-64-0P, 4-[3-(N-Methylcarbamoyl)phenoxy]-1-nitrobenzene 77992-50-8P, 4-Bromo-3-(trifluoromethyl)aniline hydrochloride 119431-22-0P, 3-Chloro-4-(2,2,2-trifluoroacetylamino)phenol 153435-79-1P, N-Methyl-3-bromobenzenesulfonamide 176977-85-8P, Methyl 4-chloropyridine-2-carboxylate hydrochloride 220000-87-3P, 4-Chloro-N-methyl-2-pyridinecarboxamide 228401-15-8P, 2-(N-(Benzyloxycarbonyl)amino)-3-methoxynaphthalene 228401-43-2P, 4-(3-Methoxycarbonyl-4-methoxyphenoxy)-1-nitrobenzene 228401-44-3P, 4-(3-Carboxy-4-methoxyphenoxy)-1-nitrobenzene 252061-66-8P, 5-Hydroxyisoindolin-1-one 284461-73-0P 284461-89-8P 284462-37-9P, 4-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]aniline 284462-38-0P, 5-(4-Nitrophenoxy)isoindoline-1,3-dione 284462-39-1P, 5-(4-Aminophenoxy)isoindoline-1,3-dione 284462-40-4P, 1-(4-tert-Butyl-2-nitrophenyl)-2,5-dimethylpyrrole 284462-41-5P, 5-tert-Butyl-2-(2,5-dimethylpyrrolyl)aniline 284462-42-6P, 4-[[2-(N-Methylcarbamoyl)-4-pyridyl]oxy]-2-methylaniline hydrochloride 284462-43-7P 284462-44-8P 284462-45-9P, 4-Chloro-2-methoxy-5-(trifluoromethyl)aniline 284462-46-0P, 4-[3-(N-Methylcarbamoyl)-4-methoxyphenoxy]-1-nitrobenzene 284462-47-1P, 4-[3-(N-Methylcarbamoyl)-4-methoxyphenoxy]aniline 284462-48-2P, 5-(4-Nitrophenoxy)-2-methylisoindoline-1,3-dione 284462-49-3P, 5-(4-Aminophenoxy)-2-methylisoindoline-1,3-dione 284462-51-7P, 4-Chloro-2-[N-(2-morpholin-4-ylethyl)carbamoyl]pyridine 284462-52-8P 284462-53-9P, 4-(1-Oxoisoindolin-5-yloxy)-1-nitrobenzene 284462-54-0P, 4-(1-Oxoisoindolin-5-yloxy)aniline 284462-55-1P, 4-(3-Ethoxycarbonylphenoxy)-1-nitrobenzene 284462-56-2P, 4-[3-(N-Methylcarbamoyl)phenoxy]aniline 284462-57-3P 284462-58-4P 284462-59-5P 284462-60-8P, 4-[3-(N-Methylsulfamoyl)phenoxy]-1-nitrobenzene 284462-61-9P, 4-[3-(N-Methylsulfamoyl)phenoxy]aniline 284462-62-0P 284462-63-1P, 4-Chloro-N-[2-(triisopropylsilyloxy)ethyl]pyridine-2-carboxamide 284462-64-2P 284462-65-3P, 4-[[2-(Methoxycarbonyl)pyridin-5-yl]oxy]-1-nitrobenzene 284462-66-4P 284462-67-5P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'(4-aminophenyl)Urea 284462-68-6P, N-[4-Chloro-3-(trifluoromethyl)phenyl]-N'(4-ethoxycarbonylphenyl)Urea 284462-69-7P 284462-70-0P 284462-71-1P 284462-84-6P, 4-(4-Methylsulfonylphenoxy)-1-aniline 284462-97-1P 284670-98-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of ω-carboxy(hetero)aryl substituted di-Ph urea raf kinase inhibitors by reacting arylisocyanates with arylamines)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 62 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:493376 HCAPLUS Full-text

DOCUMENT NUMBER: 133:120155

TITLE: Preparation of ω-carboxy aryl substituted diphenyl ureas as p38 kinase inhibitors

INVENTOR(S): Riedl, Bernd; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Monahan, Mary-Katherine; Natero, Reina; Renick, Joel; Sibley, Robert N.

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000041698	A1	20000720	WO 2000-US768	20000113 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2359244	A1	20000720	CA 2000-2359244	20000113 <--
EP 1158985	A1	20011205	EP 2000-905597	20000113 <--
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US 20030139605	A1	20030724	US 2002-71248	20020211 <--
US 20030105091	A1	20030605	US 2002-86417	20020304 <--
AU 2004200566	A1	20040311	AU 2004-200566	20040213 <--
AU 2004200566	B2	20060817		
AU 2004200722	A1	20040318	AU 2004-200722	20040224 <--
AU 2004200722	B2	20080110		
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PRIORITY APPLN. INFO.:			US 1999-115878P	P 19990113 <--
			US 1999-257265	A2 19990225 <--
			US 1999-425229	A2 19991022 <--
			US 1999-115877P	P 19990113 <--
			US 1999-257266	B2 19990225 <--
			US 1999-425228	B1 19991022 <--
			AU 2000-25016	A3 20000112 <--
			AU 2000-27250	A3 20000113 <--
			WO 2000-US768	W 20000113 <--
			US 2001-948915	A1 20010910 <--
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OTHER SOURCE(S):	MARPAT 133:120155			

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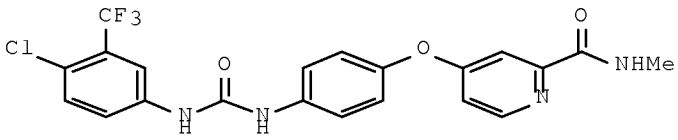


II

AB The title compds. ADB [I; D = NHCONH; A = substituted moiety of up to 40 carbon atoms of the formula L(ML1)q (wherein L = 5-6 membered cyclic structure; L1 = substituted cyclic moiety having at least 5 members; M = bridging group having al least one atom; q = 1-3; each of L and L1 contains 0-4 members of the group consisting of N, O and S); B = (un)substituted up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the

group consisting of N, O and S], useful in treating p38 mediated diseases, were prepared E.g., a multi-step synthesis of the urea II which showed IC50 of 1-10 μM against p38, was given. Compds. I are effective at 0.01-200 mg/kg/day (oral administration).

IT 284462-06-2P

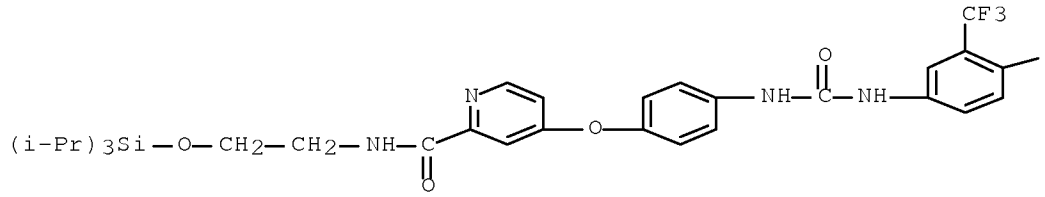
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of ω-carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)

RN 284462-06-2 HCAPLUS

CN 2-Pyridinecarboxamide, 4-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]amino]phenoxy]-N-[2-[[tris(1-methylethyl)silyl]oxy]ethyl]- (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

IC ICM A61K031-535

ICS A61K031-50; A61K031-445; A61K031-44; A61K031-40; A61K031-34; A61K031-17

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 1

IT 284461-86-5P 284461-89-8P 284462-06-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of ω-carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)

IT 228418-48-2P 284461-33-2P 284461-34-3P 284461-35-4P 284461-36-5P
284461-37-6P 284461-38-7P 284461-39-8P 284461-40-1P 284461-41-2P
284461-42-3P 284461-43-4P 284461-44-5P
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284461-55-8P 284461-56-9P 284461-57-0P 284461-58-1P
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284462-33-5P 284462-34-6P 284462-35-7P 284462-36-8P
284462-70-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ω-carboxy aryl substituted di-Ph ureas as p38 kinase inhibitors)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 63 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:421667 HCAPLUS Full-text
DOCUMENT NUMBER: 131:58659
TITLE: Preparation of diaryl ureas as inhibitors of p38 kinase.
INVENTOR(S): Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Hatoum-Mokdad, Holia; Rodriguez, Mareli; Sibley, Robert; Wang, Ming
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932463	A1	19990701	WO 1998-US27265	19981222 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2315715	A1	19990701	CA 1998-2315715	19981222 <--
AU 9919399	A	19990712	AU 1999-19399	19981222 <--
EP 1042305	A1	20001011	EP 1998-964221	19981222 <--
EP 1042305	B1	20050608		
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JP 2001526276	T	20011218	JP 2000-525400	19981222	<--
JP 3887769	B2	20070228			
AT 297383	T	20050615	AT 1998-964221	19981222	<--
PT 1042305	T	20051031	PT 1998-964221	19981222	<--
ES 2154252	T3	20051201	ES 1998-964221	19981222	<--
EP 1616865	A1	20060118	EP 2005-12144	19981222	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
MX 2000PA06227	A	20020311	MX 2000-PA6227	20000622	<--
HK 1032050	A1	20051118	HK 2001-102468	20010407	<--
AU 2003213527	A1	20030814	AU 2003-213527	20030717	<--
PRIORITY APPLN. INFO.:			US 1997-995749	A 19971222	<--
			AU 1999-19399	A3 19981222	<--
			EP 1998-964221	A3 19981222	<--
			WO 1998-US27265	W 19981222	<--

OTHER SOURCE(S): MARPAT 131:58659

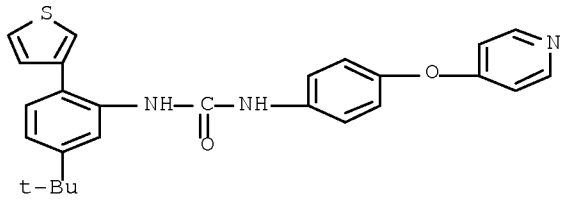
AB A method of treating a p-38 mediated disease other than cancer comprises administration of BNHCONHA [A = (substituted) Ph, pyridyl, 2-thienyl; B = (substituted) aryl, heteroaryl containing ≥1 6-membered aromatic structure containing 0-4 N, O, or S atoms]. Thus, 5-tert-butyl-2-(3-tetrahydrofuranyloxy)aniline (preparation given) and p-tolyl isocyanate were stirred 8 h in PhMe to give 75% N-(5-tert-butyl-2-(3-tetrahydrofuranyloxy)phenyl)-N'-(4-methylphenyl)urea. Title compds. inhibited p38 kinase with IC50 = 1-10 μM.

IT 228399-44-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diaryl ureas as inhibitors of p38 kinase)

RN 228399-44-8 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-(3-thienyl)phenyl]-N'-[4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)



IC ICM C07D273-00
ICS C07D275-00; A61K031-17

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 27, 28

IT 370-50-3P 117745-34-3P 228399-32-4P 228399-33-5P 228399-34-6P
228399-35-7P 228399-38-0P 228399-44-8P 228399-45-9P
228399-61-9P 228399-62-0P 228399-63-1P 228399-65-3P 228399-66-4P
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diaryl ureas as inhibitors of p38 kinase)

IT 228399-41-5 228418-48-2 228418-49-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of diaryl ureas as inhibitors of p38 kinase)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 64 OF 84 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:421642 HCAPLUS Full-text
DOCUMENT NUMBER: 131:58658
TITLE: Inhibition of raf kinase using symmetrical and unsymmetrical substituted diphenyl ureas
INVENTOR(S): Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Rodriguez, Mareli; Wang, Ming
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932436	A1	19990701	WO 1998-US26081	19981222 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,

TR, TT, UA, UG, UZ, VN, YU, ZW
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AU 9919054	A	19990712	AU 1999-19054	19981222	<--
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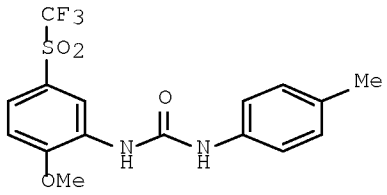
EP 1049664	A1	20001108	EP 1998-963809	19981222	<--
EP 1049664	B1	20050316			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
TR 200002616	T2	20001121	TR 2000-2616	19981222	<--
TR 200100874	T2	20010621	TR 2001-874	19981222	<--
HU 2000004437	A2	20010628	HU 2000-4437	19981222	<--
JP 2001526258	T	20011218	JP 2000-525373	19981222	<--
BR 9814375	A	20020521	BR 1998-14375	19981222	<--
NZ 505843	A	20030630	NZ 1998-505843	19981222	<--
EP 1449834	A2	20040825	EP 2003-26051	19981222	<--
EP 1449834	A3	20041222			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
RU 2247109	C2	20050227	RU 2000-120165	19981222	<--
AT 291011	T	20050415	AT 1998-963809	19981222	<--
ES 2153809	T3	20050716	ES 1998-963809	19981222	<--
PL 195808	B1	20071031	PL 1998-342078	19981222	<--
NO 2000003230	A	20000821	NO 2000-3230	20000621	<--
MX 2000PA06231	A	20020918	MX 2000-PA6231	20000622	<--
IN 2000MN00150	A	20050715	IN 2000-MN150	20000704	<--
BG 104599	A	20010330	BG 2000-104599	20000712	<--
BG 64594	B1	20050831			
IN 2003MN00960	A	20050429	IN 2003-MN960	20031013	<--

PRIORITY APPLN. INFO.:	US 1997-996344	A	19971222	<--
	EP 1998-963809	A3	19981222	<--
	WO 1998-US26081	W	19981222	<--

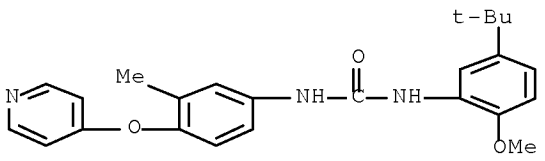
OTHER SOURCE(S): MARPAT 131:58658
GI



II

AB The invention relates to the use of a group of aryl ureas ANHCONHB [I; A = certain (un)substituted Ph, pyridinyl, or thien-2-yl groups; B = certain (un)substituted mono- to tricyclic aryl or heteroaryl groups] in treating raf-mediated diseases, and pharmaceutical compns. for use in such therapy. A subset of I are novel and are claimed per se. Approx. 160 invention compds. and numerous intermediates were prepared For instance, reaction of tolyl isocyanate with 2-methoxy-5-(trifluoromethanesulfonyl)aniline in EtOAc gave title compound II. In an in vitro raf kinase assay, all compds. displayed IC50 values between 1 nM and 10 μM.

IT 228399-40-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)
RN 228399-40-4 HCAPLUS
CN Urea, N-[5-(1,1-dimethylethyl)-2-methoxyphenyl]-N'-[3-methyl-4-(4-pyridinyloxy)phenyl]- (CA INDEX NAME)



IC ICM C07C275-24
ICS C07D213-02; C07D333-02; A61K031-17; A61K031-38; A61K031-44
CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 7
IT 370-50-3P 228399-32-4P 228399-33-5P 228399-34-6P 228399-35-7P
228399-36-8P 228399-38-0P 228399-39-1P 228399-40-4P
228399-41-5P 228399-42-6P 228399-43-7P 228399-44-8P
228399-45-9P 228399-47-1P 228399-48-2P 228399-49-3P
228399-50-6P 228399-51-7P 228399-52-8P
228399-53-9P 228399-54-0P 228399-56-2P 228399-57-3P
228399-58-4P 228399-59-5P 228399-60-8P 228399-61-9P
228399-62-0P 228399-63-1P 228399-65-3P 228399-66-4P 228399-67-5P
228399-68-6P 228399-69-7P 228399-70-0P 228399-71-1P 228399-72-2P
228399-74-4P 228399-75-5P 228399-76-6P 228399-77-7P
228399-78-8P 228399-79-9P 228399-80-2P 228399-82-4P 228399-83-5P
228399-84-6P 228399-85-7P 228399-86-8P 228399-87-9P 228399-88-0P
228399-89-1P 228399-90-4P 228399-92-6P 228399-93-7P
228399-94-8P 228399-95-9P 228399-96-0P 228399-97-1P
228399-98-2P 228399-99-3P 228400-01-9P 228400-02-0P
228400-03-1P 228400-04-2P 228400-05-3P 228400-06-4P 228400-07-5P
228400-08-6P 228400-10-0P 228400-11-1P 228400-12-2P
228400-13-3P 228400-14-4P 228400-15-5P 228400-16-6P 228400-17-7P
228400-18-8P 228400-20-2P 228400-21-3P 228400-22-4P
228400-23-5P 228400-24-6P 228400-25-7P 228400-26-8P
228400-27-9P 228400-28-0P 228400-30-4P 228400-31-5P 228400-32-6P
228400-33-7P 228400-34-8P 228400-35-9P 228400-36-0P 228400-37-1P
228400-38-2P 228400-39-3P 228400-40-6P 228400-41-7P 228400-42-8P
228400-43-9P 228400-44-0P 228400-45-1P 228400-46-2P
228400-47-3P 228400-48-4P 228400-49-5P 228400-50-8P
228400-51-9P 228400-52-0P 228400-53-1P 228400-54-2P 228400-55-3P
228400-56-4P 228400-57-5P 228400-58-6P 228400-60-0P
228400-61-1P 228400-62-2P 228400-63-3P 228400-64-4P
228400-65-5P 228400-66-6P 228400-67-7P 228400-69-9P 228400-70-2P
228400-71-3P 228400-72-4P 228400-73-5P 228400-74-6P 228400-75-7P
228400-76-8P 228400-77-9P 228400-78-0P
228400-79-1P 228400-80-4P 228400-81-5P
228400-82-6P 228400-83-7P 228400-84-8P
228400-85-9P 228400-87-1P 228400-89-3P 228400-91-7P
228400-92-8P 228400-93-9P 228400-94-0P 228400-95-1P 228400-96-2P
228400-97-3P 228400-99-5P 228401-00-1P 228401-01-2P 228401-02-3P

228401-03-4P 228401-04-5P 228401-06-7P 228401-07-8P 228401-49-8P
228401-50-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sym. and unsym. substituted di-Ph ureas with inhibitory effects on tumors mediated by raf kinase)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 65 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:591849 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600585463
TITLE: Synthesis of iodine-123 labeled raf kinase inhibitor: A potential SPECT agent.
AUTHOR(S): Kabalka, George W. [Reprint Author]; Mereddy, Arjun R.; Schuller, Hildegard
CORPORATE SOURCE: Univ Tennessee, Dept Chem, Knoxville, TN 37996 USA
kabalka@utk.edu; amereddy@mc.utmck.edu
SOURCE: Abstracts of Papers American Chemical Society, (MAR 26 2006) Vol. 231, pp. 309-MEDI.
Meeting Info.: 231st National Meeting of the American-Chemical-Society. Atlanta, GA, USA. March 26 -30, 2006. Amer Chem Soc.
CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Nov 2006
Last Updated on STN: 8 Nov 2006
CC General biology - Symposia, transactions and proceedings 00520
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Diagnostic 12504
Pathology - Therapy 12512
Respiratory system - Pathology 16006
Pharmacology - General 22002
Neoplasms - Diagnostic methods 24001
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
IT Major Concepts
Pharmacology; Methods and Techniques; Tumor Biology; Enzymology (Biochemistry and Molecular Biophysics)
IT Diseases
lung cancer: respiratory system disease, neoplastic disease, diagnosis, mortality
Lung Neoplasms (MeSH)
IT Chemicals & Biochemicals
BAY 43-9006: antineoplastic-drug, enzyme inhibitor-drug; iodine-123; raf kinase inhibitor; BAY 43-9006
radioiodinated analouge: antineoplastic-drug
IT Methods & Equipment
SPECT imaging [single photon emission computed tomography imaging]: laboratory techniques, diagnostic techniques, clinical techniques, imaging and microscopy techniques
GT USA (North America, Nearctic region)
RN 284461-73-0 (BAY 43-9006)
15715-08-9 (iodine-123)

L110 ANSWER 66 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:663269 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600657401
TITLE: Sorafenib for the treatment of renal cell carcinoma.
AUTHOR(S): Hughes, Caren L. [Reprint Author]; Tan, Winston W.; Ferrone, Marcus
CORPORATE SOURCE: Univ Texas, MD Anderson Canc Ctr, Div Pharm, Unit 90,1515 Holcombe Blvd, Houston, TX 77030 USA
calhughes@mdanderson.com
SOURCE: Journal of Pharmacy Technology, (SEP-OCT 2006) Vol. 22, No. 5, pp. 281-288.
CODEN: JPTEEB. ISSN: 8755-1225.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Nov 2006
Last Updated on STN: 29 Nov 2006

AB Objective: To summarize the pharmacology, development, and clinical application of sorafenib, a specific tyrosine kinase and vascular growth factor inhibitor, for the treatment of renal cell carcinoma (RCC).Data Sources: Clinical literature, including both primary studies and review articles, was obtained by searching MEDLINE (1966-May 2006), using the search terms BAY 43-9006, sorafenib, renal cell carcinoma, and tyrosine kinase inhibitor. Additional information was supplied by the manufacturer, Bayer HealthCare Pharmaceuticals.Study Selection and Data Extraction: Review articles, abstracts, and clinical studies related to sorafenib were analyzed. An evaluation of the research exploring sorafenib as a potential therapy for RCC was conducted. Relevant information was then selected and is reviewed in this article.Data Synthesis: Knowledge of the cellular abnormalities that can cause solid tumors has led to the development of medications that block these pathways. Sorafenib is an oral tyrosine kinase inhibitor that both blocks the Raf kinase pathway and inhibits vascular growth factors. Phase I and II trials have demonstrated that sorafenib has activity against RCC. Dermatologic reactions (rash, desquarnation), fatigue, and hypertension have been the most commonly seen treatment-related adverse events. Sorafenib received FDA approval in December 2005 for treatment of advanced RCC.Conclusions: Sorafenib is a novel oral tyrosine kinase inhibitor effective in the treatment of RCC.

CC Cytology - Animal 02506
Cytology - Human 02508
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Urinary system - Physiology and biochemistry 15504
Urinary system - Pathology 15506
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Toxicology - Pharmacology 22504
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts
Pharmacology; Oncology (Human Medicine, Medical Sciences); Urology (Human Medicine, Medical Sciences)

IT Parts, Structures, & Systems of Organisms
renal cell: excretory system

IT Diseases
renal cell carcinoma: urologic disease, neoplastic disease, drug therapy
Carcinoma, Renal Cell (MeSH); Kidney Neoplasms (MeSH)

IT Chemicals & Biochemicals
tyrosine kinase; vascular growth factor; BAY 43-9006: antineoplastic-drug; sorafenib: antineoplastic-drug, enzyme

inhibitor-drug, dosage, adverse effect, pharmacokinetics, Beyer Healthcare Pharmaceuticals, phase II clinical trial, phase I clinical trial

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 80449-02-1 (tyrosine kinase)
284461-73-0 (BAY 43-9006)

L110 ANSWER 67 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:42184 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600031990
TITLE: Targeted agents for the treatment of advanced renal cell carcinoma.
AUTHOR(S): Stadler, Walter M. [Reprint Author]
CORPORATE SOURCE: Univ Chicago, Div Genitourinary Oncol, Hematol Oncol Sect, Dept Med, Chicago, IL 60637 USA
wstadler@medicine.bsd.uchicago.edu
SOURCE: Cancer, (DEC 1 2005) Vol. 104, No. 11, pp. 2323-2333.
CODEN: CANCAR. ISSN: 0008-543X.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Dec 2005
Last Updated on STN: 28 Dec 2005

AB Metastatic renal cell carcinoma (RCC) is currently one of the most treatment-resistant malignancies. However, the elucidation of the molecular mechanisms underlying RCC development has led to the identification of promising targets for novel therapeutic agents. The involvement of the Von Hippel-Lindau protein pathway in clear cell RCC suggests that downstream targets of this pathway, namely, signaling through vascular endothelial growth factor (VEGF) in endothelial cells, platelet-derived growth factor (PDGF) in endothelial cells and pericytes, and the epidermal growth factor receptor (EGFR) pathway in tumor cells are all reasonable and rational therapeutic targets. A number of agents are in development that target VEGF (bevacizumab, a recombinant, humanized monoclonal antibody) or its receptor, VEGFR (PTK787, SU011248, and BAY 43-9006, all of which are small molecule inhibitors). Agents targeting EGFR also are being investigated clinically (gefitinib, cetuximab, erlotinib, and ABX-EGF). The Raf/MEK/ERK pathway is an important downstream convergence point for signaling through VEGFR, platelet-derived growth factor receptor (PDGFR), and EGFR (all have receptor tyrosine kinase activity) and also has important antiapoptotic effects, thereby providing an attractive target for intervention. In addition to inhibiting VEGFR and PDGFR-mediated angiogenic pathways, BAY 43-9006 has been shown to inhibit the Raf/MEK/ERK pathway at the level of Raf kinase. MEK-directed therapeutic approaches are also in development. Given that multiple molecular pathways are implicated in tumor cell growth, antitumor activity may be increased by using individual agents that target multiple pathways, or by combining different agents to allow vertical or horizontal inhibition of relevant pathways.

CC Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - Proteins, peptides and amino acids 10064
Enzymes - General and comparative studies: coenzymes 10802
Pathology - General 12502

Pathology - Therapy 12512
Urinary system - Physiology and biochemistry 15504
Urinary system - Pathology 15506
Endocrine - General 17002
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Urinary system 22032
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
IT Major Concepts
Pharmacology; Enzymology (Biochemistry and Molecular Biophysics); Oncology (Human Medicine, Medical Sciences); Nephrology (Human Medicine, Medical Sciences)
IT Parts, Structures, & Systems of Organisms
renal cell: excretory system; endothelial cell: excretory system; pericyte: excretory system
IT Diseases
metastatic renal cell carcinoma: urologic disease, neoplastic disease, drug therapy, pathology
Carcinoma, Renal Cell (MeSH); Kidney Neoplasms (MeSH); Neoplasm Metastasis (MeSH)
IT Chemicals & Biochemicals
Raf kinase [EC 2.7.1.37]; vascular endothelial growth factor [VEGF]; Raf; extracellular regulated kinase [ERK]; mitogen activated protein kinase kinase [MEK] [EC 2.7.1.37]; bevacizumab: antineoplastic-drug, renal-acting-drug; PTK787: antineoplastic-drug, renal-acting-drug; gefitinib: antineoplastic-drug, renal-acting-drug; cetuximab: antineoplastic-drug, renal-acting-drug; erlotinib: antineoplastic-drug, renal-acting-drug; platelet-derived growth factor receptor [PDGFR]: antiapoptotic effect; epidermal growth factor receptor [EGFR]: antiapoptotic effect; vascular endothelial growth factor receptor [VEGFR]: antiapoptotic effect; SU011248: antineoplastic-drug, renal-acting-drug; BAY 43-9006: antineoplastic-drug, renal-acting-drug, enzyme inhibitor-drug; ABX-epidermal growth factor receptor [ABX-EGF]: antineoplastic-drug, renal-acting-drug
IT Miscellaneous Descriptors
angiogenesis
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 144378-33-6 (Raf kinase)
144378-33-6 (EC 2.7.1.37)
127464-60-2 (vascular endothelial growth factor)
127464-60-2 (VEGF)
142805-58-1 (mitogen activated protein kinase kinase)
142805-58-1 (MEK)
142805-58-1 (EC 2.7.1.37)
216974-75-3 (bevacizumab)
212142-18-2 (PTK787)
184475-35-2 (gefitinib)
205923-56-4 (cetuximab)
183321-74-6 (erlotinib)
284461-73-0 (BAY 43-9006)

L110 ANSWER 68 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:264012 BIOSIS Full-text
DOCUMENT NUMBER: PREV200700274079
TITLE: BAY 43-9006 (sorafenib) is a potent inhibitor of FLT3 tyrosine kinase signaling and proliferation in AML cells.
AUTHOR(S): Auclair, Daniel [Reprint Author]; Miller, Donna; Carter, Christopher; Chang, Yong; Polony, Barbara; Zhang, Xiaomei; Yatsula, Victoria; Pickett, Walter; Housley, Timothy; Burd, Amy; Shi, Hong; Rocks, Sandy; Gedrich, Richard; Abriola, Laura; Apanovitch, Don; Enyedy, Istvan; Dumas, Jacques; Riedl, Bernd; Trail, Pamela A.; Wilhelm, Scott M.
CORPORATE SOURCE: Bayer Healthcare Pharmaceut, West Haven, CT USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (APR 2005) Vol. 46, pp. 1409.
Meeting Info.: 96th Annual Meeting of the American-Association-for-Cancer-Research. Anaheim, CA, USA. April 16 -20, 2005. Amer Assoc Canc Res.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Apr 2007
Last Updated on STN: 11 Jul 2007
CC General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Cytology - Human 02508
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
Neoplasms - Blood and reticuloendothelial neoplasms 24010
IT Major Concepts
Pharmacology; Blood and Lymphatics (Transport and Circulation); Enzymology (Biochemistry and Molecular Biophysics); Tumor Biology
IT Parts, Structures, & Systems of Organisms
blood: blood and lymphatics
IT Diseases
acute myeloid leukemia: neoplastic disease, blood and lymphatic disease
Leukemia, Myeloid (MeSH)
IT Chemicals & Biochemicals
ERK1/2; Stat5; RAF kinase; VEGFR [vascular endothelial growth factor receptor]; FLT3 tyrosine kinase: signaling; BAY 43-9006 [Sorafenib]: antineoplastic-drug, enzyme inhibitor-drug
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
MV4-11 cell line (cell_line)
HEK-293 cell line (cell_line)
RS4-11 cell line (cell_line)
EOL-1 cell line (cell_line)

Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse (common)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
RN 144378-33-6 (RAF kinase)
284461-73-0 (BAY 43-9006)
284461-73-0 (Sorafenib)

L110 ANSWER 69 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:258211 BIOSIS Full-text
DOCUMENT NUMBER: PREV200510048678
TITLE: Raf kinase as a target for anticancer therapeutics.
AUTHOR(S): Sridhar, Srikala S.; Hedley, David; Siu, Lillian L. [Reprint Author]
CORPORATE SOURCE: Univ Hlth Network, Princess Margaret Hosp, Dept Med Oncol and Hematol, 610 Univ Ave,Suite 5-210, Toronto, ON M5G 2M9, Canada
lillian.siu@uhn.on.ca
SOURCE: Molecular Cancer Therapeutics, (APR 2005) Vol. 4, No. 4, pp. 677-685.
ISSN: 1535-7163.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jul 2005
Last Updated on STN: 14 Jul 2005
AB The Ras-Raf-MEK-ERK (ERK) pathway is a logical therapeutic target because it represents a common downstream pathway for several key growth factor tyrosine kinase receptors, which are often mutated or overexpressed in human cancers. Although considered mainly growth-promoting, in certain contexts, this pathway also seems to be apoptosis-suppressing. Several novel agents targeting this pathway have now been developed and are in clinical trials. One of the most interesting new agents is BAY 43-9006. Although initially developed as a Raf kinase inhibitor, it can also target several other important tyrosine kinases including VEGFR-2, Flt-3, and c-Kit, which contributes to its antiproliferative and antiangiogenic properties. To date, encouraging results have been seen with BAY 43-9006, particularly in renal cell cancers which are highly vascular tumors. This review will provide an overview of the ERK signaling pathway in normal and neoplastic tissue, with a specific focus on novel therapies targeting the ERK pathway at the level of Raf kinase.
CC Pathology - Therapy 12512
Urinary system - Pathology 15506
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
IT Major Concepts
Pharmacology; Oncology (Human Medicine, Medical Sciences); Urology (Human Medicine, Medical Sciences)
IT Diseases
renal cancer: urologic disease, neoplastic disease, drug therapy

Kidney Neoplasms (MeSH)
IT Chemicals & Biochemicals
Raf kinase [EC 2.7.1.37]; BAY 43-9006: antineoplastic-drug, enzyme inhibitor-drug; VEGFR-2 kinase; Fit-3 kinase; c-Kit kinase
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrate
RN 144378-33-6 (Raf kinase)
144378-33-6 (EC 2.7.1.37)
284461-73-0 (BAY 43-9006)
218925-58-7 (VEGFR-2 kinase)
138359-29-2 (c-Kit kinase)

L110 ANSWER 70 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:185218 BIOSIS Full-text
DOCUMENT NUMBER: PREV200500186216
TITLE: The Raf kinase inhibitor BAY 43-9006 reduces cellular uptake of platinum compounds and cytotoxicity in human colorectal carcinoma cell lines.
AUTHOR(S): Heim, Martina; Scharifi, Mariam; Zisowsky, Jochen; Jaehde, Ulrich; Voliotis, Dimitris; Seeber, Siegfried; Strumberg, Dirk [Reprint Author]
CORPORATE SOURCE: Sch MedDept Hematol and Med Oncol, Ruhr Univ Bochum, Holkeskampring 40, D-44621, Herne, Germany
dirk.strumberg@uni-essen.de
SOURCE: Anti-Cancer Drugs, (February 2005) Vol. 16, No. 2, pp. 129-136. print.
CODEN: ANTDEV. ISSN: 0959-4973.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 May 2005
Last Updated on STN: 18 May 2005
AB Raf kinase plays a central role in oncogenic signaling and acts as a downstream effector of Ras in the extracellular signal-regulated (ERK) kinase pathway. BAY 43-9006 (BAY) is a novel signal transduction inhibitor that prevents tumor cell proliferation and angiogenesis through blockade of the Raf/MEK/ERK pathway at the level of Raf kinase and the receptor tyrosine kinases vascular endothelial growth factor receptor-2 and platelet-derived growth factor receptor-beta. The present study evaluates the effects of combining BAY and platinum derivatives on human colorectal cancer cells using different incubation protocols. Our data show that the combination of oxaliplatin or cisplatin with BAY results in marked antagonism irrespective of the used application schedule. Furthermore, BAY abrogates the cisplatin-induced G2 arrest as well as the G1 arrest induced by oxaliplatin. BAY alone arrests cancer cells in their current cell cycle phase and affects cell cycle regulative genes. Specifically, BAY reduced the protein expression of p21Cip1 as well as cyclin D1, and inhibits the expression of cdc2 (cdk1). Utilizing atom absorption spectrometry, BAY significantly reduced cellular uptake of platinum compounds and thereby the generation of DNA adducts. Taken together, co-incubation with BAY results in reduced cellular uptake of platinum compounds and consecutively reduced generation of DNA adducts, and eventually decreased cellular cytotoxicity in human colorectal cancer cells. Our results indicate that the Raf kinase inhibitor BAY 43-9006 might also directly or

indirectly interact with platinum transporter proteins in vitro. Copyright 2005 Lippincott Williams & Wilkins.

CC Genetics - General 03502
Genetics - Human 03508
Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Minerals 10069
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Pharmacology; Tumor Biology

IT Chemicals & Biochemicals
BAY 43-9006: antineoplastic-drug, enzyme inhibitor-drug; DNA; Mek; Raf kinase [EC 2.7.1.37]; cdc2; cisplatin: antineoplastic-drug; cyclin D1; extracellular signal-regulated kinase [EC 2.7.1.37]; oxaliplatin: antineoplastic-drug; p21Cip1; platelet-derived growth factor receptor-beta; platinum; vascular endothelial growth factor receptor-2

IT Methods & Equipment
atom absorption spectrometry: laboratory techniques, spectrum analysis techniques

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HCT8 cell line (cell line): human colon carcinoma cells
HT 29 cell line (cell line): human colon carcinoma cells
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 284461-73-0 (BAY 43-9006)
144378-33-6 (Raf kinase)
9026-43-1 (Raf kinase)
144378-33-6 (EC 2.7.1.37)
9026-43-1 (EC 2.7.1.37)
15663-27-1 (cisplatin)
142243-02-5 (extracellular signal-regulated kinase)
9026-43-1 (extracellular signal-regulated kinase)
142243-02-5 (EC 2.7.1.37)
9026-43-1 (EC 2.7.1.37)
61825-94-3 (oxaliplatin)
7440-06-4 (platinum)

L110 ANSWER 71 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:32325 BIOSIS Full-text
DOCUMENT NUMBER: PREV200500030385
TITLE: BAY 43-9006 exhibits broad spectrum oral antitumor activity and targets the RAF/MEK/ERK pathway and receptor tyrosine kinases involved in tumor progression and angiogenesis.
AUTHOR(S): Wilhelm, Scott M. [Reprint Author]; Carter, Christopher; Tang, Liya; Wilkie, Dean; McNabola, Angela; Rong, Hong; Chen, Charles; Zhang, Xiaomei; Vincent, Patrick; McHugh,

Mark; Cao, Yichen; Shujath, Jaleel; Gawlak, Susan; Eveleigh, Deepa; Rowley, Bruce; Liu, Li; Adnane, Lila; Lynch, Mark; Auclair, Daniel; Taylor, Ian; Gedrich, Rich; Voznesensky, Andrei; Riedl, Bernd; Post, Leonard E.; Bollag, Gideon; Trail, Pamela A.
CORPORATE SOURCE: Dept Canc Res, Bayer Pharmaceut Corp, 400 Morgan Lane, W Haven, CT, 06516, USA
scott.wilhelm.b@bayer.com
SOURCE: Cancer Research, (October 1 2004) Vol. 64, No. 19, pp. 7099-7109. print.
ISSN: 0008-5472 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Jan 2005
Last Updated on STN: 12 Jan 2005

AB The RAS/RAF signaling pathway is an important mediator of tumor cell proliferation and angiogenesis. The novel bi-aryl urea BAY 43-9006 is a potent inhibitor of Raf-1, a member of the RAF/MEK/ERK signaling pathway. Additional characterization showed that BAY 43-9006 suppresses both wild-type and V599E mutant BRAF activity in vitro. In addition, BAY 43-9006 demonstrated significant activity against several receptor tyrosine kinases involved in neovascularization and tumor progression, including vascular endothelial growth factor receptor (VEGFR)-2, VEGFR-3, platelet-derived growth factor receptor beta, Fit-3, and c-KIT. In cellular mechanistic assays, BAY 43-9006 demonstrated inhibition of the mitogen-activated protein kinase pathway in colon, pancreatic, and breast tumor cell lines expressing mutant KRAS or wild-type or mutant BRAF, whereas non-small-cell lung cancer cell lines expressing mutant KRAS were insensitive to inhibition of the mitogen-activated protein kinase pathway by BAY 43-9006. Potent inhibition of VEGFR-2, platelet-derived growth factor receptor P, and VEGFR-3 cellular receptor autophosphorylation was also observed for BAY 43-9006. Once daily oral dosing of BAY 43-9006 demonstrated broad-spectrum antitumor activity in colon, breast, and non-small-cell lung cancer xenograft models. Immunohistochemistry demonstrated a close association between inhibition of tumor growth and inhibition of the extracellular signal-regulated kinases (ERKs) 1/2 phosphorylation in two of three xenograft models examined, consistent with inhibition of the RAF/MEK/ERK pathway in some but not all models. Additional analyses of microvessel density and microvessel area in the same tumor sections using antimurine CD31 antibodies demonstrated significant inhibition of neovascularization in all three of the xenograft models. These data demonstrate that BAY 43-9006 is a novel dual action RAF kinase and VEGFR inhibitor that targets tumor cell proliferation and tumor angiogenesis.

CC Cytology - General 02502
Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Digestive system - Pathology 14006
Respiratory system - Pathology 16006
Reproductive system - Pathology 16506
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Oncology (Human Medicine, Medical Sciences); Pharmacology
IT Diseases
breast cancer: neoplastic disease, reproductive system disease/female

Breast Neoplasms (MeSH)
IT Diseases
colon cancer: digestive system disease, neoplastic disease
Colonic Neoplasms (MeSH)
IT Diseases
non-small-cell lung cancer: neoplastic disease, respiratory system disease
Carcinoma, Non-Small-Cell Lung (MeSH); Lung Neoplasms (MeSH)
IT Diseases
pancreatic cancer: digestive system disease, neoplastic disease
Pancreatic Neoplasms (MeSH)
IT Chemicals & Biochemicals
BRAF protein; Bay 43-9006: antineoplastic-drug, oral administration; CD31 antibody; Flt-3; MEK/ERK; RAF; RAS; Raf-1 [EC 2.7.1.37]; c-KIT; mitogen-activated protein kinase pathway; platelet-derived growth factor receptor beta; receptor tyrosine kinase [EC 2.7.1.112]; vascular endothelial growth factor receptor 2 [VEGFR-2]; vascular endothelial growth factor receptor 3 [VEGFR-3]
IT Methods & Equipment
cellular mechanistic assay: bioassay techniques, laboratory techniques; immunochemistry: immunologic techniques, laboratory techniques
IT Miscellaneous Descriptors
RAF/MEK/ERK signaling pathway; angiogenesis; tumor progression
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
BxPC-3 cell line (cell line)
HASMC cell line (cell line)
HEK-293 cell line (cell line)
HUVEC cell line (cell line)
LOX cell line (cell line)
MDA-MB-231 cell line (cell line)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
NIH 3T3 cell line (cell line)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
RN 284461-73-0 (Bay 43-9006)
9026-43-1 (Raf-1)
9026-43-1 (EC 2.7.1.37)
340830-03-7 (receptor tyrosine kinase)
80449-02-1 (receptor tyrosine kinase)
340830-03-7 (EC 2.7.1.112)
80449-02-1 (EC 2.7.1.112)

L110 ANSWER 72 OF 84 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:391335 BIOSIS Full-text
DOCUMENT NUMBER: PREV200400393629
TITLE: Validation of a liquid chromatography assay for the quantification of the Raf kinase inhibitor BAY 43-9006 in small volumes of mouse

serum.
AUTHOR(S): Afify, Samar; Rapp, Ulf R.; Hogger, Petra [Reprint Author]
CORPORATE SOURCE: Inst Pharm and Lebensmittelchem, Univ Wurzburg, Am Hubland, D-97074, Wurzburg, Germany
hogger@pzlc.uni-wuerzburg.de
SOURCE: Journal of Chromatography B, (September 25 2004) Vol. 809, No. 1, pp. 99-103. print.
ISSN: 1570-0232 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Oct 2004
Last Updated on STN: 6 Oct 2004

AB BAY 43-9006 is a selective Raf-1 kinase inhibitor with antitumor activity against a variety of human cancers. A highly sensitive HPLC method for determination of BAY 43-9006 in small volumes of serum (30 mul) was developed. Sample preparation involved a liquid-liquid extraction procedure with tolnaftate as internal standard followed by linear gradient elution at a reversed phase C18 column and UV detection. The method was selective and the calibration curves were linear over the concentration range of 80-2000 ng/ml. The intra-day accuracy ranged from 99.9 to 107.6% and the inter-day accuracy from 94.6 to 115%. The lower limit of quantitation (LOQ) was 80 ng/ml with an accuracy of 105.8%. Thus, this method has been validated and can be applied for the drug monitoring or pharmacokinetic studies of BAY 43-9006 in small volumes of serum samples. Copyright 2004 Elsevier B.V. All fights reserved.

CC Pathology - Therapy 12512
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Pharmacology - General 22002
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008

IT Major Concepts
Methods and Techniques; Pharmacology
IT Parts, Structures, & Systems of Organisms
serum: blood and lymphatics, small volumes
IT Diseases
cancer: neoplastic disease, drug therapy
Neoplasms (MeSH)
IT Chemicals & Biochemicals
BAY 43-9006: antineoplastic-drug, enzyme inhibitor-drug, selective Raf-1 kinase inhibitor; tolnaftate: internal standard
IT Methods & Equipment
UV detection: laboratory techniques, spectrum analysis techniques; linear gradient elution: laboratory techniques; liquid chromatography: chromatographic techniques, laboratory techniques; liquid-liquid extraction: laboratory techniques; reversed phase C-18 column: laboratory equipment
IT Miscellaneous Descriptors
calibration curves; inter-day accuracy; intra-day accuracy; lower limit of quantitation [LOQ]

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse (common)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 284461-73-0 (BAY 43-9006)
2398-96-1 (tolnaftate)

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ACCESSION NUMBER: 2003189385 EMBASE Full-text
TITLE: Clinical review 158 - Beyond radioiodine: A review of potential new therapeutic approaches for thyroid cancer.
AUTHOR: Braga-Basaria, Milena; Ringel, Matthew D., Dr. (correspondence)
CORPORATE SOURCE: Washington Hospital Center, MedStar Research Institute, Washington, DC 20010, United States. matthew.ringel@medstar.net
AUTHOR: Braga-Basaria, Milena
CORPORATE SOURCE: SEMPR, Servico de Endocrinol. e Metabologia, Univ. Federal do Parana, Curitiba 80.060-240, Brazil.
AUTHOR: Ringel, Matthew D., Dr. (correspondence)
CORPORATE SOURCE: 110 Irving Street NW, Washington, DC 20010, United States. matthew.ringel@medstar.net
AUTHOR: Ringel, Matthew D., Dr. (correspondence)
CORPORATE SOURCE: 110 Irving Street NW, Washington, DC 20010, United States. matthew.ringel@medstar.net
SOURCE: Journal of Clinical Endocrinology and Metabolism, (1 May 2003) Vol. 88, No. 5, pp. 1947-1960.
Refs: 104
ISSN: 0021-972X CODEN: JCEMAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
003 Endocrinology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 May 2003
Last Updated on STN: 29 May 2003

AB One of the greatest challenges in the management of patients with follicular cell-derived thyroid cancer is the treatment of tumors that progress despite surgery, radioiodine, and T(4) suppression of TSH. As knowledge of thyroid cancer biology improves, the potential exists to develop compounds targeted to treat thyroid cancers that do not respond to traditional therapy. Recently, the development of therapies targeted against specific molecular pathways involved in cancer progression has resulted in dramatic responses in patients with chronic myelogenous leukemia, gastrointestinal stromal tumors, and other cancers. A number of compounds are currently being evaluated in clinical trials that alter pathways involved thyroid cancer, and several of these agents have been tested in thyroid cancer in vitro and in vivo. In this review we will discuss the mechanisms of action and preclinical/clinical data for several of these compounds that have the potential to play an important role in the management of thyroid cancer in the future.

CT Medical Descriptors:
breast carcinoma: DT, drug therapy
cancer radiotherapy
clinical trial
colon carcinoma: DT, drug therapy
colorectal carcinoma: DT, drug therapy
drug activity
drug effect
drug receptor binding
gene activation
gene function

gene mutation
head and neck carcinoma: DT, drug therapy
head and neck carcinoma: RT, radiotherapy
hematologic malignancy: DT, drug therapy
human
lung carcinoma: DT, drug therapy
nonhuman
pancreas carcinoma: DT, drug therapy
priority journal
prostate carcinoma: DT, drug therapy
protein expression
review
side effect: SI, side effect
solid tumor: DT, drug therapy
*thyroid carcinoma: DT, drug therapy
*thyroid carcinoma: ET, etiology
urinary tract carcinoma: DT, drug therapy

CT Drug Descriptors:
2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: AE, adverse drug reaction
2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: CT, clinical trial
2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: DT, drug therapy
2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: PO, oral drug administration
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: CT, clinical trial
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: CB, drug combination
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: DT, drug therapy
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: PD, pharmacology
*antisense oligonucleotide: AE, adverse drug reaction
*antisense oligonucleotide: CT, clinical trial
*antisense oligonucleotide: CB, drug combination
*antisense oligonucleotide: DT, drug therapy
*antisense oligonucleotide: PD, pharmacology
bevacizumab: AE, adverse drug reaction
bevacizumab: CT, clinical trial
bevacizumab: DT, drug therapy
bevacizumab: PD, pharmacology
cgp 69846a: AE, adverse drug reaction
cgp 69846a: CT, clinical trial
cgp 69846a: DT, drug therapy
cgp 69846a: PD, pharmacology
cisplatin: CB, drug combination
cisplatin: DT, drug therapy
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
epidermal growth factor receptor: EC, endogenous compound
epidermal growth factor receptor antibody: CT, clinical trial
epidermal growth factor receptor antibody: DT, drug therapy
epidermal growth factor receptor antibody: PD, pharmacology
gemcitabine: CB, drug combination
gemcitabine: DT, drug therapy
isis 2503: AE, adverse drug reaction
isis 2503: CT, clinical trial
isis 2503: CB, drug combination

isis 2503: DT, drug therapy
isis 2503: PD, pharmacology
l 778123: AE, adverse drug reaction
l 778123: CT, clinical trial
lonafarnib: AE, adverse drug reaction
lonafarnib: CT, clinical trial
lonafarnib: CB, drug combination
lonafarnib: DT, drug therapy
manumycin: CB, drug combination
manumycin: DT, drug therapy
manumycin: PD, pharmacology
mitogen activated protein kinase inhibitor: AE, adverse drug reaction
mitogen activated protein kinase inhibitor: CT, clinical trial
mitogen activated protein kinase inhibitor: DT, drug therapy
mitogen activated protein kinase inhibitor: PO, oral drug administration
paclitaxel: CB, drug combination
paclitaxel: DT, drug therapy
paclitaxel: PD, pharmacology
phenylacetic acid: AE, adverse drug reaction
phenylacetic acid: CT, clinical trial
phenylacetic acid: IV, intravenous drug administration
phenylacetic acid: PD, pharmacology
phosphotransferase inhibitor: AE, adverse drug reaction
phosphotransferase inhibitor: CT, clinical trial
phosphotransferase inhibitor: DT, drug therapy
phosphotransferase inhibitor: PD, pharmacology
protein antibody
protein farnesyltransferase inhibitor: CT, clinical trial
*radioactive iodine: DT, drug therapy
Ras protein: EC, endogenous compound
semaxanib: DT, drug therapy
semaxanib: PD, pharmacology
sorafenib
tipifarnib: CT, clinical trial
tipifarnib: CB, drug combination
tipifarnib: DT, drug therapy
topotecan: CB, drug combination
topotecan: DT, drug therapy
trastuzumab: CT, clinical trial
trastuzumab: CB, drug combination
trastuzumab: DT, drug therapy
trastuzumab: PD, pharmacology
tyrosine kinase receptor: EC, endogenous compound
unindexed drug
vasculotropin antibody: AE, adverse drug reaction
vasculotropin antibody: CT, clinical trial
vasculotropin antibody: DT, drug therapy
vasculotropin antibody: PD, pharmacology
vasculotropin receptor: EC, endogenous compound

RN (2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide) 212631-79-3; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8; (bevacizumab) 216974-75-3; (cgp 69846a) 177075-18-2; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (doxorubicin) 23214-92-8, 25316-40-9; (gemcitabine) 103882-84-4; (isis 2503) 149957-14-2; (lonafarnib) 193275-84-2; (manumycin) 52665-74-4; (paclitaxel) 33069-62-4; (phenylacetic acid) 103-82-2; (semaxanib) 186610-95-7; (sorafenib) 284461-73-0; (tipifarnib) 192185-72-1; (topotecan) 119413-54-6, 123948-87-8; (trastuzumab) 180288-69-1; (vasculotropin receptor) 301253-48-5

CN (1) avastin; (2) isis 2503; (3) isis 5132; (4) l 778123; (5) lonafarnib; (6) semaxanib; (7) tipifarnib; (8) trastuzumab; bay 439006; bms 214662; pd 184352
CO (1) Genentech (United States); (2) Isis (United States); (3) Isis; (4) Merck and Co (United States); (5) Schering Plough (United States); (6) Sugen (United States); (7) Johnson and Johnson (United States); (8) Genentech

L110 ANSWER 74 OF 84 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003455328 EMBASE Full-text
TITLE: Tyrosine Kinase Inhibitors as Cancer Therapy.
AUTHOR: Nichols, Gwen L., Dr. (correspondence)
CORPORATE SOURCE: Department of Medicine, Division of Hematology, Columbia Univ. Coll. of Phys./Surgs., New York, NY, United States. nichols@cuccfa.ccc.columbia.edu
AUTHOR: Nichols, Gwen L., Dr. (correspondence)
CORPORATE SOURCE: 650 W. 168th St., New York, NY 10032, United States. nichols@cuccfa.ccc.columbia.edu
AUTHOR: Nichols, Gwen L., Dr. (correspondence)
CORPORATE SOURCE: 650 W. 168th St., New York, NY 10032, United States. nichols@cuccfa.ccc.columbia.edu
SOURCE: Cancer Investigation, (2003) Vol. 21, No. 5, pp. 758-771. Refs: 108
ISSN: 0735-7907 CODEN: CINVD7
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Dec 2003
Last Updated on STN: 11 Dec 2003
CT Medical Descriptors:
autocrine effect
breast cancer: DT, drug therapy
*cancer therapy
clinical trial
colorectal cancer: DT, drug therapy
enzyme activation
enzyme inhibition
gene mutation
gene overexpression
gene translocation
human
kidney carcinoma: DT, drug therapy
lung non small cell cancer: DT, drug therapy
lung small cell cancer: DT, drug therapy
melanoma: DT, drug therapy
mesothelioma: DT, drug therapy
meta analysis
ovary cancer: DT, drug therapy
paracrine signaling
phase 1 clinical trial
phase 2 clinical trial
phase 3 clinical trial
priority journal
review
signal transduction

CT Drug Descriptors:
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology
canertinib: CT, clinical trial
canertinib: DT, drug therapy
canertinib: PD, pharmacology
carboplatin: CT, clinical trial
carboplatin: CB, drug combination
carboplatin: DT, drug therapy
cyclophosphamide: CB, drug combination
cyclophosphamide: DT, drug therapy
cytarabine: CB, drug combination
cytarabine: DT, drug therapy
doxorubicin: CT, clinical trial
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
emd 55900
erlotinib: CT, clinical trial
erlotinib: DT, drug therapy
erlotinib: PD, pharmacology
etoposide: CB, drug combination
etoposide: DT, drug therapy
fluorouracil: CT, clinical trial
fluorouracil: CB, drug combination
fluorouracil: DT, drug therapy
gefitinib: CT, clinical trial
gefitinib: CB, drug combination
gefitinib: DT, drug therapy
gefitinib: PD, pharmacology
gemcitabine: CT, clinical trial
gemcitabine: CB, drug combination
gemcitabine: DT, drug therapy
homoharringtonine: CT, clinical trial
homoharringtonine: CB, drug combination
homoharringtonine: DT, drug therapy
humv 833: CT, clinical trial
humv 833: DT, drug therapy
humv 833: PD, pharmacology
hydroxyurea: CB, drug combination
hydroxyurea: DT, drug therapy
imatinib: CT, clinical trial
imatinib: CB, drug combination
imatinib: DT, drug therapy
imatinib: PD, pharmacology
interferon: CT, clinical trial
interferon: CB, drug combination
interferon: DT, drug therapy
irinotecan: CT, clinical trial
irinotecan: CB, drug combination
irinotecan: DT, drug therapy
oxaliplatin: CT, clinical trial
oxaliplatin: CB, drug combination
oxaliplatin: DT, drug therapy
paclitaxel: CT, clinical trial
paclitaxel: CB, drug combination
paclitaxel: DT, drug therapy

pelitinib: CT, clinical trial
pelitinib: DT, drug therapy
pelitinib: PD, pharmacology
phthalazine derivative: CT, clinical trial
phthalazine derivative: DT, drug therapy
phthalazine derivative: PD, pharmacology
*protein tyrosine kinase inhibitor: CT, clinical trial
*protein tyrosine kinase inhibitor: CB, drug combination
*protein tyrosine kinase inhibitor: DT, drug therapy
*protein tyrosine kinase inhibitor: PD, pharmacology
quinazoline derivative: CT, clinical trial
quinazoline derivative: DT, drug therapy
quinazoline derivative: PD, pharmacology
semaxanib: CT, clinical trial
semaxanib: CB, drug combination
semaxanib: DT, drug therapy
semaxanib: PD, pharmacology
sorafenib: CT, clinical trial
sorafenib: DT, drug therapy
sorafenib: PD, pharmacology
taxane derivative: CT, clinical trial
taxane derivative: CB, drug combination
taxane derivative: DT, drug therapy
trastuzumab: CT, clinical trial
trastuzumab: CB, drug combination
trastuzumab: DT, drug therapy
unclassified drug
unindexed drug
vandetanib: CT, clinical trial
vandetanib: DT, drug therapy
vandetanib: PD, pharmacology

RN (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (carboplatin) 41575-94-4; (cyclophosphamide) 50-18-0; (cytarabine) 147-94-4, 69-74-9; (doxorubicin) 23214-92-8, 25316-40-9; (erlotinib) 183319-69-9, 183321-74-6; (etoposide) 33419-42-0; (fluorouracil) 51-21-8; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gemcitabine) 103882-84-4; (homoharringtonine) 26833-87-4; (hydroxyurea) 127-07-1; (imatinib) 152459-95-5, 220127-57-1; (irinotecan) 100286-90-6; (oxaliplatin) 61825-94-3; (paclitaxel) 33069-62-4; (pelitinib) 257933-82-7; (semaxanib) 186610-95-7; (sorafenib) 284461-73-0; (trastuzumab) 180288-69-1; (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3

CN bay 43 9006; ci 1033; ekb 569; emd 55900; humv 833; iressa; osi 774; sti 571; su 5416; su 6668; zd 1839; zd 6474

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ACCESSION NUMBER: 2003471818 EMBASE Full-text
TITLE: Pharmacogenetic candidate genes for melanoma.
AUTHOR: Hull, Christopher; Leachman, Sancy (correspondence)
CORPORATE SOURCE: Department of Dermatology, Univ. of Utah School of Medicine, Salt Lake City, UT, United States. sancy.leachman@hci.utah.edu
AUTHOR: Larson, April; Leachman, Sancy (correspondence)
CORPORATE SOURCE: Huntsman Cancer Institute, Salt Lake City, UT, United States. sancy.leachman@hci.utah.edu
SOURCE: Pharmacogenomics, (Nov 2003) Vol. 4, No. 6, pp. 753-765. Refs: 140
ISSN: 1462-2416 CODEN: PARMFL

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 013 Dermatology and Venereology
016 Cancer
022 Human Genetics
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Dec 2003
Last Updated on STN: 4 Dec 2003

AB The incidence of melanoma is rising at an alarming rate and has become an important public health concern. If detected early, melanoma carries an excellent prognosis after appropriate surgical resection. Unfortunately, advanced melanoma has a poor prognosis and is notoriously resistant to radiation and chemotherapy. The relative resistance of melanoma to a wide-range of chemotherapeutic agents and high toxicity of current therapies has prompted a search for effective alternative treatments that would improve prognosis and limit side effects. Advances in molecular genetics are revealing in increasing detail the mechanisms responsible for the development of melanoma. Hopefully, elucidation of these pathways will provide a means of screening high-risk individuals and allow new drug development for prevention and treatment by identification of specific pharmacological targets. This review will summarize the genetics of melanoma with the goal of providing insights into potential pharmacogenetic candidate genes.

CT Medical Descriptors:
adverse drug reaction
cancer chemotherapy
cancer incidence
cancer prevention
cancer radiotherapy
cancer screening
cancer surgery
drug targeting
high risk patient
human
*melanoma: DI, diagnosis
*melanoma: DT, drug therapy
*melanoma: ET, etiology
*melanoma: PC, prevention
*melanoma: SU, surgery
molecular genetics
nonhuman
*pharmacogenetics
prognosis
public health
retrospective study
review
skin carcinogenesis

CT Drug Descriptors:
5 aza 2' deoxycytidine: DT, drug therapy
7 hydroxystaurosporine: DT, drug therapy
7 hydroxystaurosporine: PD, pharmacology
ARF protein: EC, endogenous compound
cyclin dependent kinase inhibitor: PD, pharmacology
flavopiridol: DT, drug therapy
flavopiridol: PD, pharmacology
helix loop helix protein: EC, endogenous compound
imatinib: PD, pharmacology
melanocortin 1 receptor: EC, endogenous compound
phosphatidylinositol 3,4,5 trisphosphate 3 phosphatase: EC, endogenous

compound
protein farnesyltransferase inhibitor: PD, pharmacology
protein inhibitor: PD, pharmacology
protein inhibitor: TP, topical drug administration
protein p16
protein p53: EC, endogenous compound
protein tyrosine kinase inhibitor: PD, pharmacology
Raf protein: EC, endogenous compound
Ras protein: EC, endogenous compound
roscovitine: DT, drug therapy
roscovitine: PD, pharmacology
sorafenib: PD, pharmacology
unclassified drug

RN (5 aza 2' deoxycytidine) 2353-33-5; (7 hydroxystaurosporine) 112953-11-4; (flavopiridol) 131740-09-5, 146426-40-6; (imatinib) 152459-95-5, 220127-57-1; (melanocortin 1 receptor) 234764-00-2, 234764-02-4; (roscovitine) 186692-46-6; (sorafenib) 284461-73-0

CN (1) gleevec; bay 439006

CO (1) Novartis; Aventis; Cyclacel; Kyowa Hakko Kogyo

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ACCESSION NUMBER: 2003437254 EMBASE Full-text
TITLE: Targeting HIF-1 for cancer therapy.
AUTHOR: Semenza, Gregg L. (correspondence)
CORPORATE SOURCE: McKusick-Nathans Inst. Genetic Med., Johns Hopkins University, School of Medicine, Baltimore, MD 21287-3914, United States. gsemenza@jhmi.edu
SOURCE: Nature Reviews Cancer, (Oct 2003) Vol. 3, No. 10, pp. 721-732.
Refs: 107
ISSN: 1474-175X CODEN: NRCAC4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Nov 2003
Last Updated on STN: 13 Nov 2003

AB Hypoxia-inducible factor 1 (HIF-1) activates the transcription of genes that are involved in crucial aspects of cancer biology, including angiogenesis, cell survival, glucose metabolism and invasion. Intratumoral hypoxia and genetic alterations can lead to HIF-1α overexpression, which has been associated with increased patient mortality in several cancer types. In preclinical studies, inhibition of HIF-1 activity has marked effects on tumour growth. Efforts are underway to identify inhibitors of HIF-1 and to test their efficacy as anticancer therapeutics.

CT Medical Descriptors:
angiogenesis
cell invasion
cell proliferation
cell survival
clinical trial
drug efficacy
*drug targeting
enzyme activation
gene activity
gene expression

gene function
gene mutation
gene overexpression
*gene targeting
genetic transcription
glucose metabolism
human
hypoxia
metastasis
nonhuman
oncogene
oncogene neu
priority journal
protein binding
protein degradation
protein modification
*protein targeting
review
signal transduction
tissue oxygenation
transcription regulation
treatment failure
tumor growth

CT Drug Descriptors:
1 benzyl 3 (5 hydroxymethyl 2 furyl)indazole: PD, pharmacology
1 methylpropyl 2 imidazolyl disulfide: PD, pharmacology
17 allylaminogeldanamycin: CT, clinical trial
17 allylaminogeldanamycin: PD, pharmacology
2 (2 amino 3 methoxyphenyl)chromone: PD, pharmacology
2 methoxyestradiol: CT, clinical trial
2 methoxyestradiol: PD, pharmacology
antineoplastic agent: CT, clinical trial
antineoplastic agent: PD, pharmacology
camptothecin: PD, pharmacology
celecoxib: CT, clinical trial
celecoxib: PD, pharmacology
erlotinib: CT, clinical trial
erlotinib: PD, pharmacology
G protein coupled receptor: EC, endogenous compound
gefitinib: CT, clinical trial
gefitinib: PD, pharmacology
*hypoxia inducible factor 1: EC, endogenous compound
hypoxia inducible factor 1alpha: EC, endogenous compound
imatinib: PD, pharmacology
mitogen activated protein kinase: EC, endogenous compound
phosphatidylinositol 3 kinase: EC, endogenous compound
pleurotin: PD, pharmacology
protein tyrosine kinase inhibitor: PD, pharmacology
sorafenib: CT, clinical trial
sorafenib: PD, pharmacology
temsirolimus: CT, clinical trial
temsirolimus: PD, pharmacology
topotecan: PD, pharmacology
trastuzumab: PD, pharmacology
ubiquitin protein ligase: EC, endogenous compound
unclassified drug

RN (1 benzyl 3 (5 hydroxymethyl 2 furyl)indazole) 170632-47-0; (2 (2 amino 3 methoxyphenyl)chromone) 167869-21-8; (2 methoxyestradiol) 362-07-2; (camptothecin) 7689-03-4; (celecoxib) 169590-42-5; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6,

184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (mitogen activated protein kinase) 142243-02-5; (phosphatidylinositol 3 kinase) 115926-52-8; (sorafenib) 284461-73-0; (temsirolimus) 162635-04-3, 343261-52-9; (topotecan) 119413-54-6, 123948-87-8; (trastuzumab) 180288-69-1; (ubiquitin protein ligase) 134549-57-8

CN bay 439006; cci 779; glivec; herceptin; iressa; osi 774; pd 98059; yc 1; zd 1839

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ACCESSION NUMBER: 2004088284 EMBASE Full-text

TITLE: Targeted therapy for epithelial ovarian cancer: Current status and future prospects.

AUTHOR: See, H.T. (correspondence); Kavanagh, John J.; Hu, W.; Bast Jr., R.C.

CORPORATE SOURCE: Dept. of Gynecol. Medical Oncology, Univ. TX M. D. Anderson Cancer Ctr., Houston, TX, United States. jkavanag@mdanderson.org

AUTHOR: Kavanagh, John J.

CORPORATE SOURCE: Dept. of Gynecologic Med. Oncology, M. D. Anderson Cancer Center, Unit 401, 1515 Holcombe Boulevard, Houston, TX 77030-4009, United States. jkavanag@mdanderson.org

AUTHOR: See, H.T. (correspondence)

CORPORATE SOURCE: Dept. of Gynecologic Med. Oncology, MD Anderson Cancer Center, Box 401, 1515, Holcombe Boulevard, Houston, TX 77030, United States.

SOURCE: International Journal of Gynecological Cancer, (Nov 2003) Vol. 13, No. 6, pp. 701-734.
Refs: 268
ISSN: 1048-891X CODEN: IJGCEN

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 010 Obstetrics and Gynecology
016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 11 Mar 2004
Last Updated on STN: 11 Mar 2004

AB Despite advances in surgery and chemotherapy, less than 20% of patients with stage III or IV ovarian cancer survive long-term. In the past, cytotoxic regimens have been developed empirically, combining active agents at maximally tolerated doses, often without a clear rationale for their interaction. Advances in understanding the biology of ovarian cancer have identified multiple molecular targets that differ in normal and malignant cells. Targets include cell cycle regulators, growth factor receptors, signal transduction pathways, molecules that confer drug resistance, and angiogenic mechanisms. A number of targeted agents have entered clinical trials. Small molecular weight inhibitors, monoclonal antibodies, and antisense and gene therapy are all being evaluated alone and in combination with cytotoxic drugs. In contrast to earlier studies, the impact of each agent on the designated target can be assessed and agents can be matched to the genotype and phenotype of malignant and normal cells. In the long run, this should facilitate individualization of more effective, less toxic therapy for women with ovarian cancer.

CT Medical Descriptors:
abdominal cramp: SI, side effect
acne: SI, side effect

*angiogenesis
animal model
anorexia: SI, side effect
*apoptosis
cancer combination chemotherapy
cancer immunotherapy
cancer survival
cell cycle
cell growth
cell immortalization
cheilitis: SI, side effect
chemotherapy induced emesis: SI, side effect
clinical trial
dermatitis: ET, etiology
diarrhea: SI, side effect
drug approval
drug mechanism
*drug targeting
enzyme activation
epithelium cell
fatigue: SI, side effect
female
*gene therapy
growth regulation
gynecologic cancer: DR, drug resistance
gynecologic cancer: DT, drug therapy
gynecologic cancer: ET, etiology
human
human cell
hypertension: SI, side effect
interstitial lung disease: SI, side effect
major clinical study
meta analysis
metastasis: CO, complication
mouse
multicenter study
multidrug resistance
myalgia: SI, side effect
nausea: SI, side effect
neurotoxicity: SI, side effect
neutropenia: SI, side effect
nonhuman
oncogene
oncogene neu
*ovary cancer: DR, drug resistance
*ovary cancer: DT, drug therapy
*ovary cancer: ET, etiology
phase 1 clinical trial
phase 2 clinical trial
phase 3 clinical trial
priority journal
proteinuria: SI, side effect
pruritus: SI, side effect
rash: SI, side effect
review
sensory neuropathy: SI, side effect
signal transduction
skin toxicity: ET, etiology
skin toxicity: SI, side effect
suicide gene therapy

thorax pain: SI, side effect
thrombocytopenia: SI, side effect
viral gene therapy
vomiting: SI, side effect
CT Drug Descriptors:
2 morpholino 8 phenylchromone: CB, drug combination
2 morpholino 8 phenylchromone: DT, drug therapy
2 morpholino 8 phenylchromone: TO, drug toxicity
2 morpholino 8 phenylchromone: PD, pharmacology
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: AE, adverse drug reaction
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: AD, drug administration
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PO, oral drug administration
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology
5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: AE, adverse drug reaction
5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: CT, clinical trial
5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: AD, drug administration
5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: DT, drug therapy
5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: PO, oral drug administration
5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide: PD, pharmacology
*antineoplastic agent: AE, adverse drug reaction
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: AD, drug administration
*antineoplastic agent: CB, drug combination
*antineoplastic agent: CM, drug comparison
*antineoplastic agent: DO, drug dose
*antineoplastic agent: IT, drug interaction
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: TO, drug toxicity
*antineoplastic agent: IP, intraperitoneal drug administration
*antineoplastic agent: IV, intravenous drug administration
*antineoplastic agent: PO, oral drug administration
*antineoplastic agent: PK, pharmacokinetics
*antineoplastic agent: PD, pharmacology
antisense oligonucleotide
atrasentan: AE, adverse drug reaction
atrasentan: CT, clinical trial
atrasentan: AD, drug administration
atrasentan: DT, drug therapy
atrasentan: IP, intraperitoneal drug administration
atrasentan: PD, pharmacology
bevacizumab: AE, adverse drug reaction
bevacizumab: CT, clinical trial
bevacizumab: AD, drug administration
bevacizumab: DT, drug therapy
bevacizumab: IV, intravenous drug administration
bevacizumab: PD, pharmacology

bortezomib: AE, adverse drug reaction
bortezomib: CT, clinical trial
bortezomib: CB, drug combination
bortezomib: DO, drug dose
bortezomib: DT, drug therapy
bortezomib: PD, pharmacology
*canfosfamide: CT, clinical trial
*canfosfamide: AD, drug administration
*canfosfamide: CB, drug combination
*canfosfamide: DO, drug dose
*canfosfamide: DT, drug therapy
*canfosfamide: IV, intravenous drug administration
*canfosfamide: PD, pharmacology
cetuximab: CT, clinical trial
cetuximab: CB, drug combination
cetuximab: IT, drug interaction
cetuximab: DT, drug therapy
cetuximab: PD, pharmacology
cgp 69846a: CT, clinical trial
cgp 69846a: DT, drug therapy
cgp 69846a: PD, pharmacology
cisplatin: AE, adverse drug reaction
cisplatin: CT, clinical trial
cisplatin: CB, drug combination
cisplatin: CM, drug comparison
cisplatin: DT, drug therapy
epidermal growth factor receptor
erlotinib: AE, adverse drug reaction
erlotinib: CT, clinical trial
erlotinib: AD, drug administration
erlotinib: CM, drug comparison
erlotinib: DT, drug therapy
erlotinib: PO, oral drug administration
erlotinib: PK, pharmacokinetics
erlotinib: PD, pharmacology
gefitinib: AE, adverse drug reaction
gefitinib: CT, clinical trial
gefitinib: AD, drug administration
gefitinib: DT, drug therapy
gefitinib: PO, oral drug administration
gefitinib: PD, pharmacology
imatinib: CT, clinical trial
imatinib: DT, drug therapy
imatinib: PD, pharmacology
isi 3521
isis 3521: AE, adverse drug reaction
isis 3521: CT, clinical trial
isis 3521: DO, drug dose
isis 3521: DT, drug therapy
isis 3521: PD, pharmacology
*ispinesib: CT, clinical trial
*ispinesib: DT, drug therapy
*ispinesib: PD, pharmacology
*monoclonal antibody: AE, adverse drug reaction
*monoclonal antibody: CT, clinical trial
*monoclonal antibody: AD, drug administration
*monoclonal antibody: CB, drug combination
*monoclonal antibody: IT, drug interaction
*monoclonal antibody: DT, drug therapy
*monoclonal antibody: IV, intravenous drug administration

*monoclonal antibody: PD, pharmacology
ONYX 015
peginterferon: CT, clinical trial
peginterferon: CB, drug combination
peginterferon: IT, drug interaction
peginterferon: DT, drug therapy
protein kinase C inhibitor: AE, adverse drug reaction
protein kinase C inhibitor: CT, clinical trial
protein kinase C inhibitor: DO, drug dose
protein kinase C inhibitor: DT, drug therapy
protein kinase C inhibitor: PD, pharmacology
protein tyrosine kinase inhibitor: CT, clinical trial
protein tyrosine kinase inhibitor: AD, drug administration
protein tyrosine kinase inhibitor: DT, drug therapy
protein tyrosine kinase inhibitor: PO, oral drug administration
protein tyrosine kinase inhibitor: PK, pharmacokinetics
protein tyrosine kinase inhibitor: PD, pharmacology
*sorafenib: AE, adverse drug reaction
*sorafenib: CT, clinical trial
*sorafenib: AD, drug administration
*sorafenib: DT, drug therapy
*sorafenib: PO, oral drug administration
*sorafenib: PK, pharmacokinetics
*sorafenib: PD, pharmacology
tamoxifen: CT, clinical trial
tamoxifen: CM, drug comparison
tamoxifen: DT, drug therapy
tanomastat: CT, clinical trial
tanomastat: DT, drug therapy
tanomastat: PD, pharmacology
thalidomide: CT, clinical trial
thalidomide: CM, drug comparison
thalidomide: DT, drug therapy
tipifarnib: AE, adverse drug reaction
tipifarnib: CT, clinical trial
tipifarnib: AD, drug administration
tipifarnib: DT, drug therapy
tipifarnib: PO, oral drug administration
tipifarnib: PD, pharmacology
trastuzumab: CT, clinical trial
trastuzumab: CB, drug combination
trastuzumab: IT, drug interaction
trastuzumab: DT, drug therapy
trastuzumab: PD, pharmacology
unclassified drug
unindexed drug
vatalanib: AD, drug administration
vatalanib: DT, drug therapy
vatalanib: PO, oral drug administration
vatalanib: PK, pharmacokinetics
vatalanib: PD, pharmacology
virus vector

RN (2 morpholino 8 phenylchromone) 154447-36-6; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (5 amino 1 [3,5 dichloro 4 (4 chlorobenzoyl)benzyl] 1h 1,2,3 triazole 4 carboxamide) 99519-84-3; (atrasentan) 173864-34-1, 173937-91-2, 195733-43-8; (bevacizumab) 216974-75-3; (bortezomib) 179324-69-7, 197730-97-5; (canfosfamide) 158382-37-7, 439943-59-6; (cetuximab) 205923-56-4; (cgp 69846a) 177075-18-2; (cisplatin) 15663-27-1, 26035-31-4, 96081-74-2; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2,

184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (isis 3521) 151879-73-1; (ispinesib) 336113-53-2, 514820-03-2; (sorafenib) 284461-73-0; (tamoxifen) 10540-29-1; (tanomastat) 179545-76-7, 179545-77-8; (thalidomide) 50-35-1; (tipifarnib) 192185-72-1; (trastuzumab) 180288-69-1; (vatalanib) 212141-54-3, 212142-18-2

CN (1) avastin; (2) erbitux; (3) gleevec; (4) herceptin; (5) imc c225; (6) iressa; (7) ONYX 015; (8) osi 774; (9) ps 341; (10) r 115777; (11) sti 571; (12) tarceva; (13) tlk 286; (14) velcade; (15) zarnestra; (16) zd 1839; bay 12 9566; bay 43 9006; isi 3521; isis 5132; ly 294002; ptk 787; sb 715992; su 6668

CO (1) Genentech (United States); (2) Imclone (United States); (3) Novartis (Switzerland); (4) Genentech (United States); (5) Imclone (United States); (6) Astra Zeneca (United Kingdom); (7) Onyx (United States); (8) Osi (United States); (9) Millennium Pharmaceuticals (United States); (10) Johnson and Johnson (United States); (11) Novartis (Switzerland); (12) Osi (United States); (13) Telik (United States); (14) Millennium Pharmaceuticals (United States); (15) Johnson and Johnson (United States); (16) Astra Zeneca (United Kingdom)

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ACCESSION NUMBER: 2003481481 EMBASE Full-text
TITLE: The impact of anti-angiogenic agents on cancer therapy.
AUTHOR: Marme, Dieter (correspondence)
CORPORATE SOURCE: Tumor Biology Center, Institute of Molecular Oncology, Breisacherstrasse 117, 79106 Freiburg, Germany. marme@tumorbio.uni-freiburg.de
SOURCE: Journal of Cancer Research and Clinical Oncology, (Nov 2003) Vol. 129, No. 11, pp. 607-620.
Refs: 89
ISSN: 0171-5216 CODEN: JCROD7
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Dec 2003
Last Updated on STN: 29 Dec 2003

CT Medical Descriptors:
angiogenesis
breast cancer: DT, drug therapy
*cancer: DT, drug therapy
*cancer chemotherapy
cancer combination chemotherapy
cancer inhibition
cancer model
cell transformation
clinical trial
colorectal cancer: DT, drug therapy
drug effect
drug efficacy
drug mechanism
drug potency
drug safety
drug targeting
drug tolerability
endothelium cell
glioblastoma: DT, drug therapy

human
IC 50
kidney carcinoma: DT, drug therapy
leukemia: DT, drug therapy
liver metastasis: CO, complication
liver metastasis: DT, drug therapy
lung hemorrhage: SI, side effect
lung non small cell cancer: DT, drug therapy
melanoma: DT, drug therapy
nonhodgkin lymphoma: DT, drug therapy
nonhuman
oncogene
pancreas cancer: DT, drug therapy
priority journal
protein family
radioimmunotherapy
regulatory mechanism
review
side effect: SI, side effect
signal transduction
stem cell
tumor growth
tumor suppressor gene
tumor vascularization
CT Drug Descriptors:
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: AE, adverse drug reaction
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology
4 (4 fluoro 2 methyl 5 indolyloxy) 6 methoxy 7 [3 (1 pyrrolidinyl)propoxy]quinazoline: CT, clinical trial
4 (4 fluoro 2 methyl 5 indolyloxy) 6 methoxy 7 [3 (1 pyrrolidinyl)propoxy]quinazoline: DT, drug therapy
4 (4 fluoro 2 methyl 5 indolyloxy) 6 methoxy 7 [3 (1 pyrrolidinyl)propoxy]quinazoline: PD, pharmacology
5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one
5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one dimethylglycine ester: CT, clinical trial
5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one dimethylglycine ester: DT, drug therapy
5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one dimethylglycine ester: PO, oral drug administration
5,6,7,13 tetrahydro 12 (3 hydroxypropyl) 9 isopropoxymethylindeno[2,1 a]pyrrolo[3,4 c]carbazol 5(12h) one dimethylglycine ester: PD, pharmacology
a 422885 66
aal 993
ag 13925
alpha2b interferon: CB, drug combination
alpha2b interferon: DT, drug therapy
alpha2b interferon: PD, pharmacology
*angiogenesis inhibitor: AE, adverse drug reaction

*angiogenesis inhibitor: CT, clinical trial
*angiogenesis inhibitor: CB, drug combination
*angiogenesis inhibitor: CM, drug comparison
*angiogenesis inhibitor: DO, drug dose
*angiogenesis inhibitor: DT, drug therapy
*angiogenesis inhibitor: PO, oral drug administration
*angiogenesis inhibitor: PK, pharmacokinetics
*angiogenesis inhibitor: PD, pharmacology
angiozyme: CT, clinical trial
angiozyme: CB, drug combination
angiozyme: DT, drug therapy
angiozyme: PD, pharmacology
antineoplastic agent: AE, adverse drug reaction
antineoplastic agent: CT, clinical trial
antineoplastic agent: CB, drug combination
antineoplastic agent: CM, drug comparison
antineoplastic agent: DO, drug dose
antineoplastic agent: DT, drug therapy
antineoplastic agent: PO, oral drug administration
antineoplastic agent: PD, pharmacology
axitinib: CT, clinical trial
axitinib: CB, drug combination
axitinib: DT, drug therapy
axitinib: PD, pharmacology
bevacizumab: AE, adverse drug reaction
bevacizumab: CT, clinical trial
bevacizumab: CB, drug combination
bevacizumab: DT, drug therapy
bevacizumab: PD, pharmacology
bsf 466895
carbazole derivative: CT, clinical trial
carbazole derivative: DT, drug therapy
carbazole derivative: PO, oral drug administration
carbazole derivative: PD, pharmacology
cetuximab
chir 258
cilengitide: AE, adverse drug reaction
cilengitide: CT, clinical trial
cilengitide: DO, drug dose
cilengitide: DT, drug therapy
cilengitide: PK, pharmacokinetics
cilengitide: PD, pharmacology
cnt 095
cp 547 632: AE, adverse drug reaction
cp 547 632: CT, clinical trial
cp 547 632: DT, drug therapy
cp 547 632: PD, pharmacology
docetaxel: CB, drug combination
docetaxel: DT, drug therapy
docetaxel: PD, pharmacology
e 7080
emd 7200
erlotinib
gefitinib: DT, drug therapy
gefitinib: PD, pharmacology
gw 2286
gw 654652
imatinib
imc 1c11
isis 3521

isothiazole derivative: AE, adverse drug reaction
isothiazole derivative: CT, clinical trial
isothiazole derivative: DT, drug therapy
isothiazole derivative: PD, pharmacology
krn 633
l 19
ll 4
midostaurin
monoclonal antibody DC101: CT, clinical trial
monoclonal antibody DC101: DT, drug therapy
monoclonal antibody DC101: PD, pharmacology
monoclonal antibody IMC 1C11: CT, clinical trial
monoclonal antibody IMC 1C11: DT, drug therapy
monoclonal antibody IMC 1C11: PD, pharmacology
monoclonal antibody lm 609: CT, clinical trial
monoclonal antibody lm 609: DT, drug therapy
monoclonal antibody lm 609: PD, pharmacology
n acetylcolchinol phosphate
pd 166285
PD 173074
  protein tyrosine kinase inhibitor: AE, adverse drug reaction
  protein tyrosine kinase inhibitor: CT, clinical trial
  protein tyrosine kinase inhibitor: CB, drug combination
  protein tyrosine kinase inhibitor: CM, drug comparison
  protein tyrosine kinase inhibitor: DO, drug dose
  protein tyrosine kinase inhibitor: DT, drug therapy
  protein tyrosine kinase inhibitor: PO, oral drug administration
  protein tyrosine kinase inhibitor: PD, pharmacology
receptor antibody: CT, clinical trial
receptor antibody: DT, drug therapy
receptor antibody: PD, pharmacology
rwj 417975
sorafenib
su 11657
sunitinib: CT, clinical trial
sunitinib: DT, drug therapy
sunitinib: PD, pharmacology
temozolomide: CM, drug comparison
temozolomide: DT, drug therapy
temozolomide: PD, pharmacology
trastuzumab: DT, drug therapy
trastuzumab: PD, pharmacology
unclassified drug
unindexed drug
vandetanib: CT, clinical trial
vandetanib: DT, drug therapy
vandetanib: PD, pharmacology
vasculotropin antibody: CM, drug comparison
vasculotropin antibody: DT, drug therapy
vasculotropin antibody: PD, pharmacology
vasculotropin receptor 2 antibody: CT, clinical trial
vasculotropin receptor 2 antibody: DT, drug therapy
vasculotropin receptor 2 antibody: PD, pharmacology
vasculotropin receptor 2 inhibitor: AE, adverse drug reaction
vasculotropin receptor 2 inhibitor: CT, clinical trial
vasculotropin receptor 2 inhibitor: DT, drug therapy
vasculotropin receptor 2 inhibitor: PO, oral drug administration
vasculotropin receptor 2 inhibitor: PD, pharmacology
vasculotropin trap: CT, clinical trial
vasculotropin trap: CM, drug comparison

vasculotropin trap: DT, drug therapy
vasculotropin trap: PK, pharmacokinetics
vasculotropin trap: PD, pharmacology
vatalanib: CT, clinical trial
vatalanib: CB, drug combination
vatalanib: DO, drug dose
vatalanib: DT, drug therapy
vatalanib: PD, pharmacology
zk 260 255

RN (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (alpha2b interferon) 99210-65-8; (axitinib) 319460-85-0; (bevacizumab) 216974-75-3; (cetuximab) 205923-56-4; (cilengitide) 188968-51-6; (docetaxel) 114977-28-5; (erlotinib) 183319-69-9, 183321-74-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (gw 2286) 601517-74-2; (imatinib) 152459-95-5, 220127-57-1; (isis 3521) 151879-73-1; (midostaurin) 120685-11-2; (n acetylcolchinol phosphate) 219923-05-4; (sorafenib) 284461-73-0; (sunitinib) 341031-54-7, 557795-19-4; (temozolomide) 85622-93-1; (trastuzumab) 180288-69-1; (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3; (vatalanib) 212141-54-3, 212142-18-2

CN (1) a 422885 66; (2) aal 993; (3) ag 013736; (4) ag 13925; (5) azd 2171; (6) azd 6474; (7) bay 43 9006; (8) bsf 466895; (9) cep 7055; (10) cep 7055; (11) chir 258; (12) cnt 095; (13) cp 547 632; (14) e 7080; (15) emd 121974; (16) emd 7200; (17) emd 7200; (18) gleevec; (19) gw 2286; (20) gw 654652; (21) herceptin; (22) imc 1c11; (23) imc c225; (24) iressa; (25) isis 3521; (26) isis 3521; (27) krn 633; (28) l 19; (29) ll 4; (30) pd 166285; (31) PD 173074; (32) pkc 412; (33) ptk 787; (34) ptk 787; (35) rwj 417975; (36) su 11248; (37) su 11657; (38) su 6668; (39) tarceva; (40) tarceva; (41) tarceva; (42) tsu 68; (43) vitaxin; (44) zd 6126; (45) zk 222584; (46) zk 222584; (47) zk 260 255; cep 5214

CO (1) Abbott (United States); (2) Novartis; (3) Pfizer (United States); (4) Agouron (United States); (5) Astra Zeneca (United Kingdom); (6) Astra Zeneca (United Kingdom); (7) Bayer (United States); (8) Abbott (United States); (9) Cephalon (United States); (10) Sanofi Synthelabo (France); (11) Chiron (United States); (12) Centocor (United States); (13) Pfizer (United States); (14) Eisai (Japan); (15) Merck (Denmark); (16) Bms (United States); (17) Merck (Denmark); (18) Novartis; (19) Glaxo Wellcome (United States); (20) Glaxo SmithKline (United States); (21) Genentech; (22) Glaxo SmithKline (United States); (23) Imclone (United States); (24) Astra Zeneca (United Kingdom); (25) Isis (United States); (26) Novartis; (27) Kirin (Japan); (28) university of zurich; (29) University College London (United Kingdom); (30) Pfizer (United States); (31) Pfizer (United States); (32) Novartis; (33) Novartis (Germany); (34) Schering (Germany); (35) RW Johnson (United States); (36) Sugen (United States); (37) Sugen (United States); (38) Sugen (United States); (39) Genentech (United States); (40) Hoffmann La Roche; (41) Osi (United States); (42) Taiko (Japan); (43) Medimmune (United States); (44) Astra Zeneca (United Kingdom); (45) Novartis (Germany); (46) Schering (Germany); (47) Novartis; albert einstein (United States); Bristol Myers Squibb (United States); indiana university (United States); Oxigene (United States); peregrine (United States); Regeneron (United States); Ribozyme Pharmaceuticals (United States); scribbs clinic (United States)

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ACCESSION NUMBER: 2003500287 EMBASE Full-text
TITLE: Highlights of the 39th Annual Meeting of the American Society of Clinical Oncology.
AUTHOR: Prescott, Lawrence M.
SOURCE: P and T, (Aug 2003) Vol. 28, No. 8, pp. 528-531.

ISSN: 1052-1372 CODEN: PPTTEK
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Dec 2003
Last Updated on STN: 29 Dec 2003

AB More than 25,000 oncologists, research scientists, cancer nurses, and other health care professionals from around the world gathered at the 39th Annual Meeting of the American Society of Clinical Oncology, held in Chicago, Illinois, from May 31 to June 3, 2003, to hear the latest developments in the epidemiology, prevention, diagnosis, and treatment of a variety of cancers. The most recent studies included novel therapeutic combinations and new chemotherapeutic and biological agents for the treatment of metastatic breast cancer, bronchoalveolar cell carcinoma, pancreatic cancer, colorectal cancer, melanoma, and hematologic malignancies as well as advances in the management of chemotherapy-induced adverse effects.

CT Medical Descriptors:
advanced cancer: DT, drug therapy
*anemia: DT, drug therapy
*anemia: SI, side effect
bone marrow toxicity: SI, side effect
breast cancer: DT, drug therapy
*cancer: DT, drug therapy
*cancer chemotherapy
cancer combination chemotherapy
*cancer immunotherapy
cancer survival
chemotherapy induced emesis: SI, side effect
chronic lymphatic leukemia: DT, drug therapy
clinical trial
colorectal cancer: DT, drug therapy
conference paper
diarrhea: SI, side effect
drug efficacy
drug safety
febrile neutropenia: SI, side effect
fever: SI, side effect
human
lung alveolus cell carcinoma: DT, drug therapy
lymphadenopathy: SI, side effect
major clinical study
melanoma: DT, drug therapy
metastasis: CO, complication
metastasis: DT, drug therapy
multicenter study
nausea: SI, side effect
neuropathy: SI, side effect
neutropenia: SI, side effect
nonhodgkin lymphoma: DT, drug therapy
pancreas cancer: DT, drug therapy
phase 1 clinical trial
phase 2 clinical trial
side effect: SI, side effect
skin toxicity: SI, side effect

treatment outcome
vomiting: SI, side effect
CT Drug Descriptors:
*antineoplastic agent: AE, adverse drug reaction
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: AD, drug administration
*antineoplastic agent: CB, drug combination
*antineoplastic agent: CM, drug comparison
*antineoplastic agent: DO, drug dose
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: IV, intravenous drug administration
*antineoplastic agent: PO, oral drug administration
*cancer vaccine: AE, adverse drug reaction
*cancer vaccine: CT, clinical trial
*cancer vaccine: AD, drug administration
*cancer vaccine: DT, drug therapy
*cancer vaccine: DL, intradermal drug administration
*cancer vaccine: PR, pharmaceutics
*cancer vaccine: SC, subcutaneous drug administration
carboplatin: AE, adverse drug reaction
carboplatin: CT, clinical trial
carboplatin: CB, drug combination
carboplatin: DO, drug dose
carboplatin: DT, drug therapy
carcinoembryonic antigen
cetuximab: CT, clinical trial
cetuximab: CB, drug combination
cetuximab: CM, drug comparison
cetuximab: DT, drug therapy
cyclophosphamide: AE, adverse drug reaction
cyclophosphamide: CT, clinical trial
cyclophosphamide: CB, drug combination
cyclophosphamide: DT, drug therapy
docetaxel: AE, adverse drug reaction
docetaxel: CT, clinical trial
docetaxel: CB, drug combination
docetaxel: DT, drug therapy
doxorubicin: AE, adverse drug reaction
doxorubicin: CT, clinical trial
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
*erlotinib: CT, clinical trial
*erlotinib: DT, drug therapy
fludarabine: CT, clinical trial
fludarabine: CB, drug combination
fludarabine: DT, drug therapy
fludarabine phosphate
fluorouracil: AE, adverse drug reaction
fluorouracil: CT, clinical trial
fluorouracil: CB, drug combination
fluorouracil: DO, drug dose
fluorouracil: DT, drug therapy
fluorouracil: IV, intravenous drug administration
folfirinox: AE, adverse drug reaction
folfirinox: CT, clinical trial
folfirinox: DO, drug dose
folfirinox: DT, drug therapy
folfirinox: IV, intravenous drug administration
granulocyte macrophage colony stimulating factor
irinotecan: AE, adverse drug reaction

irinotecan: CT, clinical trial
irinotecan: CB, drug combination
irinotecan: CM, drug comparison
irinotecan: DO, drug dose
irinotecan: DT, drug therapy
irinotecan: IV, intravenous drug administration
*monoclonal antibody: AE, adverse drug reaction
*monoclonal antibody: CT, clinical trial
*monoclonal antibody: CB, drug combination
*monoclonal antibody: CM, drug comparison
*monoclonal antibody: DT, drug therapy
nevsar
novel erythropoiesis stimulating protein: CT, clinical trial
novel erythropoiesis stimulating protein: CM, drug comparison
novel erythropoiesis stimulating protein: DO, drug dose
novel erythropoiesis stimulating protein: DT, drug therapy
oblimersen: AE, adverse drug reaction
oblimersen: CT, clinical trial
oblimersen: CB, drug combination
oblimersen: DT, drug therapy
oblimersen: PD, pharmacology
oxaliplatin: AE, adverse drug reaction
oxaliplatin: CT, clinical trial
oxaliplatin: CB, drug combination
oxaliplatin: DO, drug dose
oxaliplatin: DT, drug therapy
oxaliplatin: IV, intravenous drug administration
paclitaxel: AE, adverse drug reaction
paclitaxel: CT, clinical trial
paclitaxel: CB, drug combination
paclitaxel: DO, drug dose
paclitaxel: DT, drug therapy
prednisone: AE, adverse drug reaction
prednisone: CT, clinical trial
prednisone: CB, drug combination
prednisone: DT, drug therapy
protein bcl 2
protein kinase inhibitor: AE, adverse drug reaction
protein kinase inhibitor: CT, clinical trial
protein kinase inhibitor: AD, drug administration
protein kinase inhibitor: CB, drug combination
protein kinase inhibitor: DO, drug dose
protein kinase inhibitor: DT, drug therapy
protein kinase inhibitor: PO, oral drug administration
protein kinase inhibitor: PD, pharmacology
protein tyrosine kinase inhibitor: CT, clinical trial
protein tyrosine kinase inhibitor: DT, drug therapy
Raf protein
recombinant erythropoietin: CT, clinical trial
recombinant erythropoietin: CM, drug comparison
recombinant erythropoietin: DT, drug therapy
rituximab: AE, adverse drug reaction
rituximab: CT, clinical trial
rituximab: CB, drug combination
rituximab: DT, drug therapy
*sorafenib: AE, adverse drug reaction
*sorafenib: CT, clinical trial
*sorafenib: AD, drug administration
*sorafenib: CB, drug combination
*sorafenib: DO, drug dose

*sorafenib: DT, drug therapy
*sorafenib: PO, oral drug administration
*sorafenib: PD, pharmacology
trastuzumab: AE, adverse drug reaction
trastuzumab: CT, clinical trial
trastuzumab: CB, drug combination
trastuzumab: DT, drug therapy
TRICOM vaccine
unclassified drug
unindexed drug
vincristine: AE, adverse drug reaction
vincristine: CT, clinical trial
vincristine: CB, drug combination
vincristine: DT, drug therapy

RN (carboplatin) 41575-94-4; (cetuximab) 205923-56-4; (cyclophosphamide) 50-18-0; (docetaxel) 114977-28-5; (doxorubicin) 23214-92-8, 25316-40-9; (erlotinib) 183319-69-9, 183321-74-6; (fludarabine phosphate) 75607-67-9; (fludarabine) 21679-14-1; (fluorouracil) 51-21-8; (irinotecan) 100286-90-6; (oblimersen) 190977-41-4; (oxaliplatin) 61825-94-3; (paclitaxel) 33069-62-4; (prednisone) 53-03-2; (protein bcl 2) 219306-68-0; (recombinant erythropoietin) 113427-24-0, 122312-54-3, 130455-76-4; (rituximab) 174722-31-7; (sorafenib) 284461-73-0; (trastuzumab) 180288-69-1; (vincristine) 57-22-7

CN (1) aranesp; (2) bay 43 9006; (3) camptosar; (4) eloxatin; (5) erbitux; (6) erbitux; (7) fludara; (8) genasense; (9) herceptin; (10) paraplatin; (11) procrit; (12) rituxan; (13) rituxan; (14) tarceva; (15) taxol; (16) taxotere; (17) TRICOM vaccine; cytoxan; endoxan; nevsar

CO (1) Amgen; (2) Bayer; (3) Pharmacia; (4) Sanofi Synthelabo; (5) Imclone; (6) Merck; (7) Berlex; (8) Genta; (9) Genentech; (10) Bristol Myers Squibb; (11) Ortho; (12) Genentech; (13) Idec; (14) Genentech; (15) Bristol Myers Squibb; (16) Aventis; (17) Therion

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ACCESSION NUMBER: 2003156049 EMBASE Full-text
TITLE: Signal transduction modulators for cancer therapy: From promise to practice?.
AUTHOR: Lobbezoo, Marinus W., Dr. (correspondence); Van Kalken, Coenraad
CORPORATE SOURCE: NDDO Research Foundation, Amsterdam, Netherlands. lobbezoo@euronet.nl
AUTHOR: Giaccone, Giuseppe
CORPORATE SOURCE: VU Medical Center, Amsterdam, Netherlands.
SOURCE: Oncologist, (2003) Vol. 8, No. 2, pp. 210-213.
Refs: 3
ISSN: 1083-7159 CODEN: OCOLF6
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 9 May 2003
Last Updated on STN: 9 May 2003

CT Medical Descriptors:
cancer: DT, drug therapy
*cancer chemotherapy
clinical trial
conference paper

drug approval
drug design
drug screening
drug targeting
food and drug administration
human
priority journal
side effect: SI, side effect
*signal transduction
CT Drug Descriptors:
1,4 diamino 1,4 bis(2 aminophenylthio) 2,3 dicyanobutadiene
17 allylamino 17 demethoxygeldanamycin: DV, drug development
2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide: DV, drug development
4 [6 methoxy 7 [3 (1 piperidinyl)propoxy] 4 quinazolinyl] 1 piperazinecarboxylic acid (4 isopropoxyphenyl)amide: DV, drug development
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine
7 hydroxystaurosporine
*antineoplastic agent: AE, adverse drug reaction
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: CB, drug combination
*antineoplastic agent: DV, drug development
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: PO, oral drug administration
*antineoplastic agent: PD, pharmacology
ap23451: DV, drug development
bevacizumab: CT, clinical trial
bevacizumab: CB, drug combination
bevacizumab: DV, drug development
bevacizumab: DT, drug therapy
bevacizumab: PD, pharmacology
bortezomib
canertinib: DV, drug development
cetuximab: DV, drug development
cpd 5: DV, drug development
ct 32228: DV, drug development
erlotinib: AE, adverse drug reaction
erlotinib: CT, clinical trial
erlotinib: DV, drug development
erlotinib: DT, drug therapy
erlotinib: PD, pharmacology
flavopiridol: DV, drug development
gefitinib: AE, adverse drug reaction
gefitinib: CT, clinical trial
gefitinib: DV, drug development
gefitinib: DT, drug therapy
gefitinib: PD, pharmacology
gw 211: DV, drug development
imatinib: DV, drug development
imc 1c11: DV, drug development
imc 2c6: DV, drug development
imc ic11
matuzumab: DV, drug development
n acetylcolchinol phosphate
pertuzumab: DV, drug development
protein tyrosine kinase
semaxanib: DV, drug development
signal tranduction modulator: AE, adverse drug reaction
signal tranduction modulator: CT, clinical trial

signal tranduction modulator: CB, drug combination
signal tranduction modulator: DV, drug development
signal tranduction modulator: DT, drug therapy
signal tranduction modulator: PO, oral drug administration
signal tranduction modulator: PD, pharmacology
sorafenib: DV, drug development
sunitinib: CT, clinical trial
sunitinib: DV, drug development
sunitinib: DT, drug therapy
sunitinib: PO, oral drug administration
sunitinib: PD, pharmacology
temsirolimus: DV, drug development
tipifarnib: DV, drug development
trastuzumab: DV, drug development
unclassified drug
unindexed drug
vandetanib

RN (1,4 diamino 1,4 bis(2 aminophenylthio) 2,3 dicyanobutadiene) 109511-58-2; (2 (2 chloro 4 iodoanilino) n cyclopropylmethoxy 3,4 difluorobenzamide) 212631-79-3; (7 hydroxystaurosporine) 112953-11-4; (bevacizumab) 216974-75-3; (bortezomib) 179324-69-7, 197730-97-5; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (cetuximab) 205923-56-4; (erlotinib) 183319-69-9, 183321-74-6; (flavopiridol) 131740-09-5, 146426-40-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (matuzumab) 339186-68-4; (n acetylcolchinol phosphate) 219923-05-4; (protein tyrosine kinase) 80449-02-1; (semaxanib) 186610-95-7; (sorafenib) 284461-73-0; (sunitinib) 341031-54-7, 557795-19-4; (temsirolimus) 162635-04-3, 343261-52-9; (tipifarnib) 192185-72-1; (trastuzumab) 180288-69-1; (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3

CN ap23451; bay 43 9006; c225; cci 779; ci 1033; ci 1040; cpd 5; ct 32228; ct 53518; emd 72000; gw 211; imc 2c6; imc ic11; osi 774; pki 166; ps 341; r115777; st1571; su11248; su5416; u0126; ucn 01; zd1839; zd6126; zd6474

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ACCESSION NUMBER: 2003436243 EMBASE Full-text
TITLE: The pipeline of new anticancer agents for breast cancer treatment in 2003.
AUTHOR: Awada, A. (correspondence); Cardoso, F.; Atalay, G.; Giuliani, R.; Mano, M.; Piccart, M.J.
CORPORATE SOURCE: Jules Bordet Institute, Chemotherapy Unit, Boulevard de Waterloo 125, 1000 Brussels, Belgium. ahmad.awada@bordet.be
SOURCE: Critical Reviews in Oncology/Hematology, (Oct 2003) Vol. 48, No. 1, pp. 45-63.
Refs: 172
ISSN: 1040-8428 CODEN: CCRHEC
COUNTRY: Ireland
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Nov 2003
Last Updated on STN: 13 Nov 2003

AB In recent years, strategy in cancer therapy in general, and breast cancer in particular, has been the use of maximum tolerated doses of toxic non-specific agents as well as the investigation of a range of new agents that specifically

target tumor-related molecules, in a variety of biological pathways. The trial of chemotherapy (CT) versus chemotherapy+trastuzumab (Herceptin®) in HER-2-overexpressing metastatic breast cancer (MBC) was one of the first to use a biological agent in combination with chemotherapy with success and, together with some trials of taxanes in anthracycline-resistance patients one of the few to demonstrate an overall survival (OS) advantage in MBC. Five main molecular pathways are of particular interest in terms of new drug development in breast cancer: the estrogen receptor (ER) pathway, the tyrosine kinase signal transduction pathway, the cell cycle regulation pathway, the apoptosis pathway and the angiogenesis pathway. This review will focus on new agents, cytotoxic, hormonal and molecular-targeted, which are in advanced clinical stages of development for the treatment of MBC. .COPYRGT. 2003 Elsevier Ireland Ltd. All rights reserved.

CT Medical Descriptors:
alopecia: SI, side effect
anemia: SI, side effect
angiogenesis
anorexia: SI, side effect
antineoplastic activity
apoptosis
arthralgia: SI, side effect
asthenia: SI, side effect
blood toxicity: SI, side effect
*breast cancer: DR, drug resistance
*breast cancer: DT, drug therapy
cancer chemotherapy
cancer survival
cardiotoxicity: SI, side effect
cell cycle
chemotherapy induced emesis: SI, side effect
clinical trial
congestive heart failure: SI, side effect
constipation: SI, side effect
diarrhea: SI, side effect
drug effect
drug efficacy
drug eruption: SI, side effect
drug targeting
fatigue: SI, side effect
febrile neutropenia: SI, side effect
gastrointestinal symptom: SI, side effect
gene therapy
hand foot syndrome: SI, side effect
human
leukopenia: SI, side effect
metastasis: DT, drug therapy
mucosa inflammation: SI, side effect
myalgia: SI, side effect
nausea: SI, side effect
neuropathy: SI, side effect
neurotoxicity: SI, side effect
neutropenia: SI, side effect
peripheral neuropathy: SI, side effect
review
sensory neuropathy: SI, side effect
side effect: SI, side effect
signal transduction
stomatitis: SI, side effect
thrombocytopenia: SI, side effect
transaminitis: SI, side effect

CT Drug Descriptors:
3 (4 amino 1,3 dihydro 1,3 dioxo 2h isoindol 2 yl)glutarimide
angiogenesis inhibitor: DT, drug therapy
angiogenesis inhibitor: PD, pharmacology
anthracycline derivative: AE, adverse drug reaction
anthracycline derivative: CT, clinical trial
anthracycline derivative: CB, drug combination
anthracycline derivative: CM, drug comparison
anthracycline derivative: DT, drug therapy
anthracycline derivative: PD, pharmacology
antimetabolite: AE, adverse drug reaction
antimetabolite: CB, drug combination
antimetabolite: DT, drug therapy
antimetabolite: PO, oral drug administration
antimetabolite: PD, pharmacology
*antineoplastic agent: AE, adverse drug reaction
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: CB, drug combination
*antineoplastic agent: CM, drug comparison
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: IP, intraperitoneal drug administration
*antineoplastic agent: TU, intratumoral drug administration
*antineoplastic agent: PO, oral drug administration
*antineoplastic agent: PD, pharmacology
aromatase inhibitor: DT, drug therapy
aromatase inhibitor: PD, pharmacology
arzoxifene: DT, drug therapy
arzoxifene: PD, pharmacology
bms 184476: CT, clinical trial
bms 184476: CM, drug comparison
bms 184476: DT, drug therapy
bms 184476: PD, pharmacology
bortezomib
canertinib
cc 7085
cdc 801
cgp 69846a
cm 101
cyclooxygenase 2 inhibitor: CT, clinical trial
cyclooxygenase 2 inhibitor: DT, drug therapy
cyclooxygenase 2 inhibitor: PD, pharmacology
cytotoxic agent: AE, adverse drug reaction
cytotoxic agent: CT, clinical trial
cytotoxic agent: CB, drug combination
cytotoxic agent: CM, drug comparison
cytotoxic agent: DT, drug therapy
cytotoxic agent: IP, intraperitoneal drug administration
cytotoxic agent: TU, intratumoral drug administration
cytotoxic agent: PO, oral drug administration
cytotoxic agent: PD, pharmacology
DNA topoisomerase inhibitor: AE, adverse drug reaction
DNA topoisomerase inhibitor: CT, clinical trial
DNA topoisomerase inhibitor: DT, drug therapy
DNA topoisomerase inhibitor: PD, pharmacology
docetaxel: AE, adverse drug reaction
docetaxel: CT, clinical trial
docetaxel: CM, drug comparison
docetaxel: DT, drug therapy
docetaxel: PD, pharmacology
doxorubicin

erlotinib
fulvestrant: CT, clinical trial
fulvestrant: DT, drug therapy
fulvestrant: PD, pharmacology
gefitinib: CT, clinical trial
gefitinib: DT, drug therapy
gefitinib: PD, pharmacology
ixabepilone: AE, adverse drug reaction
ixabepilone: CT, clinical trial
ixabepilone: DT, drug therapy
ixabepilone: PD, pharmacology
lapatinib
lenalidomide
letrozole: CT, clinical trial
letrozole: CM, drug comparison
letrozole: DT, drug therapy
letrozole: PD, pharmacology
lonafarnib
marimastat
navelbine: CT, clinical trial
navelbine: DT, drug therapy
navelbine: PO, oral drug administration
navelbine: PD, pharmacology
paclitaxel: AE, adverse drug reaction
paclitaxel: CT, clinical trial
paclitaxel: CM, drug comparison
paclitaxel: DT, drug therapy
paclitaxel: PD, pharmacology
paclitaxel poliglumex: CT, clinical trial
paclitaxel poliglumex: DT, drug therapy
paclitaxel poliglumex: PD, pharmacology
pemetrexed
pk 166
platinum derivative: AE, adverse drug reaction
platinum derivative: CM, drug comparison
platinum derivative: DT, drug therapy
platinum derivative: PD, pharmacology
proteasome inhibitor: CT, clinical trial
proteasome inhibitor: DT, drug therapy
proteasome inhibitor: PD, pharmacology
raloxifene: DT, drug therapy
raloxifene: PD, pharmacology
retinoid derivative: DT, drug therapy
retinoid derivative: PD, pharmacology
rpr 109881a
rpr 116258a
sorafenib
tamoxifen: CT, clinical trial
tamoxifen: CM, drug comparison
tamoxifen: DT, drug therapy
tamoxifen: PD, pharmacology
taxane derivative: CT, clinical trial
taxane derivative: CB, drug combination
taxane derivative: DT, drug therapy
taxane derivative: PD, pharmacology
temsirolimus
tipifarnib
toremifene: DT, drug therapy
toremifene: PD, pharmacology
trabectedin: AE, adverse drug reaction

trabectedin: CT, clinical trial
trabectedin: DT, drug therapy
trabectedin: PD, pharmacology
trastuzumab: CT, clinical trial
trastuzumab: DT, drug therapy
trastuzumab: PD, pharmacology
unclassified drug
unindexed drug
vinflunine: AE, adverse drug reaction
vinflunine: CT, clinical trial
vinflunine: DT, drug therapy
vinflunine: PD, pharmacology

RN (3 (4 amino 1,3 dihydro 1,3 dioxo 2h isoindol 2 yl)glutarimide) 443912-23-0; (arzoxifene) 182133-25-1, 182133-27-3; (bortezomib) 179324-69-7, 197730-97-5; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (cgp 69846a) 177075-18-2; (cm 101) 188417-67-6; (docetaxel) 114977-28-5; (doxorubicin) 23214-92-8, 25316-40-9; (erlotinib) 183319-69-9, 183321-74-6; (fulvestrant) 129453-61-8; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (ixabepilone) 219989-84-1; (lapatinib) 231277-92-2, 388082-78-8, 437755-78-7; (lenalidomide) 191732-72-6; (letrozole) 112809-51-5; (lonafarnib) 193275-84-2; (marimastat) 154039-60-8; (navelbine) 71486-22-1; (paclitaxel poliglumex) 263351-82-2; (paclitaxel) 33069-62-4; (pemetrexed) 137281-23-3, 150399-23-8; (raloxifene) 82640-04-8, 84449-90-1; (sorafenib) 284461-73-0; (tamoxifen) 10540-29-1; (temsirolimus) 162635-04-3, 343261-52-9; (tipifarnib) 192185-72-1; (toremifene) 89778-26-7; (trabectedin) 114899-77-3; (trastuzumab) 180288-69-1; (vinflunine) 162652-95-1

CN abi 007; alimta; bay 439006; bb 2516; bms 184476; bms 247550; caelyx; cc 4047; cc 5013; cc 7085; cci 779; cdc 801; ci 1033; cm 101; ct 2103; et 743; faslodex; gw 2016; herceptin; isis 5132; myocet; osi 774; pk 166; ps 341; r 115777; rpr 109881a; rpr 116258a; sch 66336; taxotere; zd 1839

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ACCESSION NUMBER: 2003091304 EMBASE Full-text
TITLE: Protein kinase inhibitors from the urea class.
AUTHOR: Dumas, Jacques (correspondence)
CORPORATE SOURCE: Bayer Research Center, Bayer Corporation, Pharmaceutical Division, 400 Morgan Lane, West Haven, CT 06516, United States. jacques.dumas.b@bayer.com
SOURCE: Current Opinion in Drug Discovery and Development, (Sep 2002) Vol. 5, No. 5, pp. 718-727.
Refs: 74
ISSN: 1367-6733 CODEN: CODDFF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 25 Mar 2003
Last Updated on STN: 25 Mar 2003

AB Protein kinase inhibitors hold great potential as novel therapies for cancer and inflammatory disorders. While bis-aryl ureas have been reported as kinase inhibitors as early as 1996, a number of publications and patent applications appeared in the literature during the past two years. Three urea-based kinase

inhibitors are currently undergoing clinical trials. The present review summarizes available data, and provides an overview of the structure-activity relationships against a variety of kinase targets, including p38, Raf-1 and cyclin-dependent kinases.

CT Medical Descriptors:
*angiogenesis
animal model
antiinflammatory activity
antineoplastic activity
arthritis: DT, drug therapy
cancer chemotherapy
*cell cycle
clinical trial
diarrhea: SI, side effect
drug efficacy
drug protein binding
drug research
drug safety
drug structure
drug targeting
*enzyme inhibition
fatigue: SI, side effect
human
human cell
inflammation
kidney carcinoma: DT, drug therapy
liver cell carcinoma: DT, drug therapy
mouse
nonhuman
phase 1 clinical trial
phase 2 clinical trial
rash: SI, side effect
review
structure activity relation

CT Drug Descriptors:
*3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide: CT, clinical trial
*3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide: AD, drug administration
*3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide: AN, drug analysis
*3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide: CR, drug concentration
*3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide: DV, drug development
*3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide: DO, drug dose
*3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide: DT, drug therapy
*3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide: PO, oral drug administration
*3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide: PK, pharmacokinetics
*3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide: PD, pharmacology
4 [4 (4 fluorophenyl) 1 (3 phenylpropyl) 5 (4 pyridinyl) 1h imidazol 2 yl] 3 butyn 1 ol
5 (2,6 dichlorophenyl) 2 (2,4 difluorophenylthio)pyrimido[1,6 b]pyridazin 6 one: DV, drug development
antiinflammatory agent: CT, clinical trial

antiinflammatory agent: AD, drug administration
antiinflammatory agent: AN, drug analysis
antiinflammatory agent: DV, drug development
antiinflammatory agent: DO, drug dose
antiinflammatory agent: DT, drug therapy
antiinflammatory agent: IV, intravenous drug administration
antiinflammatory agent: PD, pharmacology
*cyclin dependent kinase inhibitor: CT, clinical trial
*cyclin dependent kinase inhibitor: AN, drug analysis
*cyclin dependent kinase inhibitor: DV, drug development
*cyclin dependent kinase inhibitor: PD, pharmacology
*doramapimod: CT, clinical trial
*doramapimod: AN, drug analysis
*doramapimod: DV, drug development
*doramapimod: DO, drug dose
*doramapimod: DT, drug therapy
*doramapimod: IV, intravenous drug administration
*doramapimod: PD, pharmacology
enzyme inhibitor: AE, adverse drug reaction
enzyme inhibitor: CT, clinical trial
enzyme inhibitor: AN, drug analysis
enzyme inhibitor: CR, drug concentration
enzyme inhibitor: DV, drug development
enzyme inhibitor: DO, drug dose
enzyme inhibitor: DT, drug therapy
enzyme inhibitor: PK, pharmacokinetics
enzyme inhibitor: PD, pharmacology
epidermal growth factor receptor kinase
erlotinib: CT, clinical trial
flavopiridol: CT, clinical trial
gefitinib: CT, clinical trial
imatinib: CT, clinical trial
mitogen activated protein kinase inhibitor: CT, clinical trial
mitogen activated protein kinase inhibitor: AN, drug analysis
mitogen activated protein kinase inhibitor: DV, drug development
mitogen activated protein kinase inhibitor: PD, pharmacology
*protein kinase inhibitor: AE, adverse drug reaction
*protein kinase inhibitor: CT, clinical trial
*protein kinase inhibitor: AD, drug administration
*protein kinase inhibitor: AN, drug analysis
*protein kinase inhibitor: CR, drug concentration
*protein kinase inhibitor: DV, drug development
*protein kinase inhibitor: DO, drug dose
*protein kinase inhibitor: DT, drug therapy
*protein kinase inhibitor: IV, intravenous drug administration
*protein kinase inhibitor: PO, oral drug administration
*protein kinase inhibitor: PK, pharmacokinetics
*protein kinase inhibitor: PD, pharmacology
  protein tyrosine kinase inhibitor: CT, clinical trial
  protein tyrosine kinase inhibitor: AN, drug analysis
  protein tyrosine kinase inhibitor: DV, drug development
  protein tyrosine kinase inhibitor: PD, pharmacology
quinazoline derivative: DV, drug development
ruboxistaurin: DV, drug development
rw 67657: DV, drug development
*sorafenib: AE, adverse drug reaction
*sorafenib: CT, clinical trial
*sorafenib: AD, drug administration
*sorafenib: AN, drug analysis
*sorafenib: DV, drug development

*sorafenib: DO, drug dose
*sorafenib: DT, drug therapy
*sorafenib: PO, oral drug administration
*sorafenib: PD, pharmacology
unclassified drug
*urea derivative: AE, adverse drug reaction
*urea derivative: CT, clinical trial
*urea derivative: AD, drug administration
*urea derivative: AN, drug analysis
*urea derivative: CR, drug concentration
*urea derivative: DV, drug development
*urea derivative: DO, drug dose
*urea derivative: DT, drug therapy
*urea derivative: IV, intravenous drug administration
*urea derivative: PO, oral drug administration
*urea derivative: PK, pharmacokinetics
*urea derivative: PD, pharmacology

RN (3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide) 252003-65-9; (4 [4 (4 fluorophenyl) 1 (3 phenylpropyl) 5 (4 pyridinyl) 1h imidazol 2 yl] 3 butyn 1 ol) 215303-72-3; (doramapimod) 285983-48-4; (epidermal growth factor receptor kinase) 79079-06-4; (erlotinib) 183319-69-9, 183321-74-6; (flavopiridol) 131740-09-5, 146426-40-6; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (ruboxistaurin) 169939-93-9, 169939-94-0; (sorafenib) 284461-73-0

CN (1) bay 43 9006; (2) birb 796; (3) cp 547632; (4) ly 333531; (5) osi 774; (6) rwj 67657; (7) vx 745; (8) zd 1839; glivec

CO (1) Bayer; (2) Boehringer Ingelheim; (3) Pfizer; (4) Lilly; (5) Osi; (6) RW Johnson; (7) Vertex; (8) Astra Zeneca; Amgen; Aventis; Banyu; BASF; Glaxo SmithKline; Pharmacia Upjohn; Sugen

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ACCESSION NUMBER: 2002326813 EMBASE Full-text
TITLE: The chemistry of biological processes: Editorial overview.
AUTHOR: McAlpine, James (correspondence); Culver, Kenneth; Ecker, David
CORPORATE SOURCE: Phytera Inc., 377 Plantation Street, Worcester, MA 01605, United States. aandjmcalpine@yahoo.com
SOURCE: Current Opinion in Drug Discovery and Development, (Mar 2002) Vol. 5, No. 2, pp. 191-193.
ISSN: 1367-6733 CODEN: CODDFF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Oct 2002
Last Updated on STN: 3 Oct 2002

CT Medical Descriptors:
Bifidobacterium
Clostridium
DNA vector
drug activity
*drug development
drug screening
editorial
Salmonella

CT Drug Descriptors:

2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine
adl 681
angiogenesis inhibitor
antibiotic agent
antineoplastic agent
bim 46228
canertinib
cyclin dependent kinase inhibitor
epidermal growth factor receptor
erlotinib
fluorouracil
gefitinib
imatinib
lb 42908
lonafarnib
nl 2001
paclitaxel
pelitinib
phosphotransferase inhibitor
protein kinase C inhibitor
protein tyrosine kinase inhibitor
recombinant antibody
semaxanib
sorafenib
tipifarnib
unclassified drug
unindexed drug
vancomycin
vandetanib
vatalanib

RN (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8; (canertinib) 267243-28-7, 289499-45-2, 338796-35-3; (erlotinib) 183319-69-9, 183321-74-6; (fluorouracil) 51-21-8; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (lonafarnib) 193275-84-2; (paclitaxel) 33069-62-4; (pelitinib) 257933-82-7; (semaxanib) 186610-95-7; (sorafenib) 284461-73-0; (tipifarnib) 192185-72-1; (vancomycin) 1404-90-6, 1404-93-9; (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3; (vatalanib) 212141-54-3, 212142-18-2

CN (1) adl 681; (2) bay 439006; (3) bim 46228; (4) bms 214662; (5) ci 1033; (6) ekb 569; (7) lb 42908; (8) nl 2001; (9) osi 774; (10) pki 166; (11) ptk 787; (12) r 115777; (13) sch 66336; (14) sti 571; (15) su 5416; (16) su 6668; (17) zd 1839; (18) zd 6474; taxol

CO (1) Novartis; (2) Bayer; (3) Biomeasure; (4) Bristol Myers Squibb; (5) Pfizer; (6) Wyeth Ayerst; (7) LG Chemical; (8) Nuoncology; (9) Osi; (10) Novartis; (11) Novartis; (12) Janssen; (13) Schering Plough; (14) Gleevec; (15) Sugen; (16) Sugen; (17) Astra Zeneca; (18) Astra Zeneca

L110 ANSWER 84 OF 84 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2002194397 EMBASE Full-text
TITLE: IDdb News focus.
SOURCE: Current Drug Discovery, (2002) No. MAY, pp. 13-16.
ISSN: 1472-7463 CODEN: CDDUAI

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
031 Arthritis and Rheumatism
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
008 Neurology and Neurosurgery
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Jun 2002
Last Updated on STN: 13 Jun 2002

CT Medical Descriptors:
alcoholism: DT, drug therapy
allergic rhinitis: DT, drug therapy
anemia: DT, drug therapy
anxiety neurosis: DT, drug therapy
asthma: DT, drug therapy
bladder disease: DT, drug therapy
*cancer: DT, drug therapy
cataplexy: DT, drug therapy
clinical trial
condyloma: DT, drug therapy
controlled study
drug approval
drug design
drug indication
drug manufacture
drug marketing
drug structure
heart failure: DT, drug therapy
human
influenza: DT, drug therapy
influenza: PC, prevention
kidney cancer: DT, drug therapy
narcolepsy: DT, drug therapy
non insulin dependent diabetes mellitus: DT, drug therapy
nonhodgkin lymphoma: DT, drug therapy
nose congestion: DT, drug therapy
note
osteoarthritis: DT, drug therapy
papilloma: DT, drug therapy
patent
rheumatoid arthritis: DT, drug therapy
*stroke: DT, drug therapy
thromboembolism: DT, drug therapy
thromboembolism: PC, prevention
*virus infection: DT, drug therapy
Wart virus

CT Drug Descriptors:
alpha adrenergic receptor stimulating agent: CB, drug combination
alpha adrenergic receptor stimulating agent: DT, drug therapy
antisense oligonucleotide: CT, clinical trial
antisense oligonucleotide: DT, drug therapy
apoptosis inhibitor: DT, drug therapy
arixta
beta 3 adrenergic receptor stimulating agent: CT, clinical trial
beta 3 adrenergic receptor stimulating agent: DT, drug therapy
bucindolol
camptothecin derivative: CT, clinical trial

camptothecin derivative: DT, drug therapy
carboxylic acid derivative: DT, drug therapy
celecoxib: DT, drug therapy
chir 200131
desloratadine: DT, drug therapy
DNA: CT, clinical trial
DNA: CB, drug combination
DNA: DT, drug therapy
epi 2010
fondaparinux: DT, drug therapy
histamine H1 receptor antagonist: CB, drug combination
histamine H1 receptor antagonist: DT, drug therapy
histamine H3 receptor agonist: DT, drug therapy
influenza vaccine: CT, clinical trial
influenza vaccine: DT, drug therapy
interleukin 2 receptor antibody: CT, clinical trial
interleukin 2 receptor antibody: DT, drug therapy
krp 199
loratadine: DT, drug therapy
naltrexone derivative: CT, clinical trial
naltrexone derivative: DT, drug therapy
ori 1001
ortataxel
oxybate sodium: DT, drug therapy
oxybutynin: CT, clinical trial
oxybutynin: DT, drug therapy
oxybutynin: TD, transdermal drug administration
phosphotransferase inhibitor: CT, clinical trial
phosphotransferase inhibitor: DT, drug therapy
phosphotransferase inhibitor: PO, oral drug administration
protein tyrosine kinase inhibitor: DV, drug development
protein tyrosine kinase inhibitor: DT, drug therapy
recombinant erythropoietin: DV, drug development
recombinant erythropoietin: DT, drug therapy
rituximab: CT, clinical trial
rituximab: CB, drug combination
rituximab: DT, drug therapy
rosiglitazone: DT, drug therapy
sb 418790
serine proteinase inhibitor: DV, drug development
serine proteinase inhibitor: DT, drug therapy
solabegron
sorafenib
ta hpv
taxane derivative: CT, clinical trial
taxane derivative: DT, drug therapy
unclassified drug
unindexed drug
uridine derivative: CT, clinical trial
uridine derivative: DT, drug therapy
valdecoxib: DT, drug therapy
vasopressin receptor antagonist: CT, clinical trial
vasopressin receptor antagonist: DT, drug therapy
virus vaccine: CT, clinical trial
virus vaccine: DV, drug development
virus vaccine: DT, drug therapy
wk 175
wx uk 1

RN (bucindolol) 71119-11-4; (celecoxib) 169590-42-5; (desloratadine) 100643-71-8; (DNA) 9007-49-2; (fondaparinux) 104993-28-4, 114870-03-0;

(interleukin 2 receptor antibody) 179045-86-4; (loratadine) 79794-75-5; (ortataxel) 186348-05-0, 186348-23-2; (oxybate sodium) 502-85-2; (oxybutynin) 1508-65-2, 5633-20-5; (recombinant erythropoietin) 113427-24-0, 122312-54-3, 130455-76-4; (rituximab) 174722-31-7; (rosiglitazone) 122320-73-4, 155141-29-0; (solabegron) 252920-94-8, 451470-34-1; (sorafenib) 284461-73-0; (valdecoxib) 181695-72-7

CN (1) arixta; (2) arixta; (3) avandia; (4) bay 439006; (5) bextra; (6) bextra; (7) celebrex; (8) celebrex; (9) chir 200131; (10) clarinex; (11) claritin; (12) epi 2010; (13) gw 427353; (14) idn 5109; (15) krp 199; (16) ori 1001; (17) oxytrol; (18) rituxan; (19) sb 418790; (20) ta hpv; (21) wk 175; (22) wx uk 1; (23) xyrem

CO (1) Organon; (2) Sanofi Synthelabo; (3) Glaxo SmithKline; (4) Bayer; (5) Pfizer; (6) Pharmacia; (7) Pfizer; (8) Pharmacia; (9) Chiron; (10) Schering Plough; (11) Schering Plough; (12) epigenesis; (13) Glaxo SmithKline; (14) Bayer; (15) Kyorin; (16) OriGenix Technologies; (17) Watson; (18) Dynavax; (19) Glaxo SmithKline; (20) Xenova; (21) Wilex Biotechnology; (22) Wilex Biotechnology; (23) Orphan

```
=> d his nofile

     (FILE 'HOME' ENTERED AT 10:58:16 ON 16 JUL 2008)

     FILE 'HCAPLUS' ENTERED AT 10:58:27 ON 16 JUL 2008
L1             1 SEA ABB=ON  PLU=ON  US20070142440/PN
                 D IBIB AB IT SC
                 SEL RN

     FILE 'REGISTRY' ENTERED AT 10:59:13 ON 16 JUL 2008
L2            47 SEA ABB=ON  PLU=ON  (102-56-7/BI OR 1199-46-8/BI OR 139691-76-2
                 /BI OR 144697-16-5/BI OR 150027-19-3/BI OR 176977-85-8/BI OR
                 19438-10-9/BI OR 220000-87-3/BI OR 2835-98-5/BI OR 28443-50-7/B
                 I OR 349-65-5/BI OR 372092-80-3/BI OR 400-99-7/BI OR 43115-40-8
                 /BI OR 446-36-6/BI OR 454-81-9/BI OR 53981-24-1/BI OR 67-56-1/B
                 I OR 74-89-5/BI OR 771-61-9/BI OR 7719-09-7/BI OR 80449-02-1/BI
                  OR 827025-41-2/BI OR 827025-43-4/BI OR 856424-02-7/BI OR
                 864291-02-1/BI OR 864291-04-3/BI OR 864291-06-5/BI OR 864291-08
                 -7/BI OR 864291-10-1/BI OR 864291-12-3/BI OR 864291-14-5/BI OR
                 864291-16-7/BI OR 864291-18-9/BI OR 864291-20-3/BI OR 864291-22
                 -5/BI OR 864291-24-7/BI OR 864291-26-9/BI OR 864291-28-1/BI OR
                 864291-32-7/BI OR 864291-34-9/BI OR 864291-39-4/BI OR 95-03-4/B
                 I OR 95-55-6/BI OR 95-84-1/BI OR 98-98-6/BI OR 99-76-3/BI)
L3               STRUCTURE UPLOADED
                 D
L4             1 SEA SSS SAM L3
                 D SCAN
L5            14 SEA ABB=ON  PLU=ON  L2 AND 3/N
L6             0 SEA ABB=ON  PLU=ON  L2 AND 4/N

     FILE 'STNGUIDE' ENTERED AT 11:03:11 ON 16 JUL 2008

     FILE 'REGISTRY' ENTERED AT 11:04:56 ON 16 JUL 2008
L7               STRUCTURE UPLOADED
L8               SCR 2043 AND 1918
L9             3 SEA SSS SAM L7 NOT L8
L10           16 SEA ABB=ON  PLU=ON  L2 AND 3-9/NR
                 D SCAN

     FILE 'STNGUIDE' ENTERED AT 11:39:41 ON 16 JUL 2008
                 D COST

     FILE 'REGISTRY' ENTERED AT 11:50:36 ON 16 JUL 2008
L11              STRUCTURE UPLOADED
                 D
L12           25 SEA SSS SAM L11 NOT L8
L13              SCR 2021
L14           33 SEA SSS SAM L11 AND L13 NOT L8
L15              SCR 1995 OR 2021
L16           30 SEA SSS SAM L11 AND L15 NOT L8
L17              SCR 1841
L18           50 SEA SSS SAM L11 AND L17 NOT L8

     FILE 'STNGUIDE' ENTERED AT 11:55:43 ON 16 JUL 2008

     FILE 'REGISTRY' ENTERED AT 11:56:29 ON 16 JUL 2008
L19              STRUCTURE UPLOADED
                 D
```

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L20          50 SEA SSS SAM L19 NOT L8
L21          50 SEA SSS SAM L19 AND L17 NOT L8
L22             SCR 2043 AND 1918 AND 1842
L23          48 SEA SSS SAM L19 NOT L22
L24          47 SEA ABB=ON  PLU=ON  L2 NOT 30-99/C
L25          47 SEA ABB=ON  PLU=ON  L2 NOT 35-99/C

     FILE 'STNGUIDE' ENTERED AT 12:06:12 ON 16 JUL 2008

     FILE 'REGISTRY' ENTERED AT 12:08:16 ON 16 JUL 2008
L26             STRUCTURE UPLOADED
                D
L27          50 SEA SSS SAM L26 NOT L22
L28          50 SEA SSS SAM L26 AND L15 NOT L22
L29             SCR 2043 AND 1918 AND 1842 AND 2016
L30          50 SEA SSS SAM L26 AND L15 NOT L29
L31             STRUCTURE UPLOADED
                D
L32          35 SEA SSS SAM L31 NOT L22
L33          35 SEA SSS SAM L31 AND L15 NOT L22
L34          36 SEA SSS SAM L31 AND L15 NOT L29

     FILE 'STNGUIDE' ENTERED AT 12:30:14 ON 16 JUL 2008

     FILE 'REGISTRY' ENTERED AT 12:38:18 ON 16 JUL 2008
L35             STRUCTURE UPLOADED
L36          50 SEA SSS SAM L35 AND L15 NOT L29

     FILE 'STNGUIDE' ENTERED AT 12:39:05 ON 16 JUL 2008

     FILE 'REGISTRY' ENTERED AT 12:40:08 ON 16 JUL 2008
L37             STRUCTURE UPLOADED
                D
L38          50 SEA SSS SAM L37 AND L15 NOT L29
L39             SCR 2043 AND 1918 AND 2050 AND 1842 AND 2016
L40          50 SEA SSS SAM L37 AND L15 NOT L39
L41             SCR 1995 OR 2021 OR 1841
L42          50 SEA SSS SAM L37 AND L41 NOT L39

     FILE 'STNGUIDE' ENTERED AT 12:49:58 ON 16 JUL 2008

     FILE 'STNGUIDE' ENTERED AT 12:54:24 ON 16 JUL 2008

     FILE 'REGISTRY' ENTERED AT 12:54:29 ON 16 JUL 2008
L43             STRUCTURE UPLOADED
                D
L44          50 SEA SSS SAM L43 AND L41 NOT L39
L45             STRUCTURE UPLOADED
                D
L46          50 SEA SSS SAM L45 AND L41 NOT L39

     FILE 'STNGUIDE' ENTERED AT 13:03:34 ON 16 JUL 2008

     FILE 'REGISTRY' ENTERED AT 13:17:03 ON 16 JUL 2008
L47             STRUCTURE UPLOADED
                D

Uploading L11.str
```

chain nodes :
7 8 9 22 24 25 26 27 28 29 36
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15 16 17 18 19 20 21
chain bonds :
6-7 7-8 8-9 14-22 18-22 27-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21
17-18 18-19 19-20 20-21
exact/norm bonds :
6-7 7-8 8-9 14-22 18-22 27-28
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 16-17 16-21
17-18 18-19 19-20 20-21
isolated ring systems :
containing 1 : 10 : 16 :

G1:O,S

G2:[*1],[*2],[*3],[*4],[*5]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom
22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 36:CLASS
37:Atom

L48 SCR 2043 AND 1918 AND 2050
L49 50 SEA SSS SAM L47 NOT L48
L50 1662 SEA SSS FUL L47 NOT L48
L51 14 SEA ABB=ON PLU=ON L50 AND L2
SAVE TEMP L50 NAT724REGL11/A

FILE 'HCAPLUS' ENTERED AT 13:24:34 ON 16 JUL 2008
L52 607 SEA ABB=ON PLU=ON L50
L53 584 SEA ABB=ON PLU=ON L52 AND PHARMAC?/SC,SX
L54 64 SEA ABB=ON PLU=ON L53 AND (AY<2004 OR PY<2004 OR PRY<2004)
L55 0 SEA ABB=ON PLU=ON L54 AND L1

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                E TYROSINE KINASE RECEPTORS/CT
                E E3+ALL
L56         2011 SEA ABB=ON  PLU=ON  "TYROSINE KINASE RECEPTORS"+UF/CT
L57           20 SEA ABB=ON  PLU=ON  L56 AND L52
L58           63 SEA ABB=ON  PLU=ON  L54 NOT L57
L59       334654 SEA ABB=ON  PLU=ON  TYROSINE KINASE? OR KINASE? OR KINASE
                INHIB?
L60         3212 SEA ABB=ON  PLU=ON  TIE(W)2 OR TIE2 OR VEGRF OR RAF KINASE?
L61       335008 SEA ABB=ON  PLU=ON  L59 OR L60
L62          382 SEA ABB=ON  PLU=ON  L52 AND L61
L63          382 SEA ABB=ON  PLU=ON  L52 AND L61
L64         1797 SEA ABB=ON  PLU=ON  (TIE2 OR TIE(W)2 OR VEGFR OR RAF) (W)
                (KINASE? OR KINASE INHIB?)
L65          114 SEA ABB=ON  PLU=ON  L52 AND L64
L66           52 SEA ABB=ON  PLU=ON  L63 AND  (AY<2004 OR PY<2004 OR PRY<2004)
L67           35 SEA ABB=ON  PLU=ON  L65 AND (AY<2004 OR PY<2004 OR PRY<2004)
L68           31 SEA ABB=ON  PLU=ON  L54 NOT L67
                SAVE TEMP L54 NAT724HCAP/A
L69           22 SEA ABB=ON  PLU=ON  BURGDORF L?/AU
L70           45 SEA ABB=ON  PLU=ON  BUCHSTALLER H?/AU
L71           36 SEA ABB=ON  PLU=ON  STIEBER F?/AU
L72           28 SEA ABB=ON  PLU=ON  AMENDT C?/AU
L73          202 SEA ABB=ON  PLU=ON  GREINER H?/AU
L74          150 SEA ABB=ON  PLU=ON  GRELL M?/AU
L75           38 SEA ABB=ON  PLU=ON  SIRRENBERG C?/AU
L76            3 SEA ABB=ON  PLU=ON  ZENKE K?/AU
L77           10 SEA ABB=ON  PLU=ON  (((L69 OR L70 OR L71 OR L72 OR L73 OR L74
                OR L75 OR L76)) AND L52) OR (L1 AND L52)
L78            5 SEA ABB=ON  PLU=ON  L77 NOT L54
                SAVE TEMP L78 NAT724HCAIN/A

     FILE 'REGISTRY' ENTERED AT 13:38:42 ON 16 JUL 2008
L79            1 SEA ABB=ON  PLU=ON  L50 AND (MEDLINE/LC OR BIOSIS/LC OR
                DRUGU/LC OR EMBASE/LC)

     FILE 'MEDLINE' ENTERED AT 13:39:09 ON 16 JUL 2008
L80            0 SEA ABB=ON  PLU=ON  L79

     FILE 'BIOSIS' ENTERED AT 13:39:15 ON 16 JUL 2008
L81           89 SEA ABB=ON  PLU=ON  L79
L82           34 SEA ABB=ON  PLU=ON  L81 AND L64
L83            3 SEA ABB=ON  PLU=ON  L82 AND (PREP? OR SYNTHES?)
                D TI 1-3
L84            0 SEA ABB=ON  PLU=ON  L82 AND ANGIOGENESIS INHIB?
L85            6 SEA ABB=ON  PLU=ON  L82 AND TYROSINE KINASE?
L86            8 SEA ABB=ON  PLU=ON  L83 OR L85

     FILE 'DRUGU' ENTERED AT 13:42:12 ON 16 JUL 2008
L87            0 SEA ABB=ON  PLU=ON  L79

     FILE 'EMBASE' ENTERED AT 13:42:27 ON 16 JUL 2008
L88         2050 SEA ABB=ON  PLU=ON  L79
L89          605 SEA ABB=ON  PLU=ON  L88 AND  TYROSINE KINASE?
L90            1 SEA ABB=ON  PLU=ON  L88 AND TYROSIN KINASE INHIB?
L91          165 SEA ABB=ON  PLU=ON  L88 AND L64
L92         1332 SEA ABB=ON  PLU=ON  RAF KINASE?
L93          164 SEA ABB=ON  PLU=ON  L92 AND L88
                D TI L90
L94           26 SEA ABB=ON  PLU=ON  L89 AND (PREPARAT? OR SYNTHES?)
                D TI KWIC 1-4
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L95          26 SEA ABB=ON  PLU=ON  L94 AND (PHARMAC? OR THERAP?)
L96          27 SEA ABB=ON  PLU=ON  L90 OR L94
L97           0 SEA ABB=ON  PLU=ON  L96 AND (AY<2004 OR PY<2004 OR PRY<2004)
L98          12 SEA ABB=ON  PLU=ON  L89 AND (AY<2004 OR PY<2004 OR PRY<2004)

     FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 13:48:43 ON 16 JUL 2008
L99           0 SEA ABB=ON  PLU=ON  BURGDORF LARS/AU
L100          9 SEA ABB=ON  PLU=ON  BUCHSTALLER HANS PETER/AU
L101          8 SEA ABB=ON  PLU=ON  STIEBER FRANK/AU
L102          7 SEA ABB=ON  PLU=ON  AMENDT CHRISTIANE/AU
L103         14 SEA ABB=ON  PLU=ON  GREINER HARTMUT/AU
L104         70 SEA ABB=ON  PLU=ON  GRELL MATTHIAS/AU
L105         19 SEA ABB=ON  PLU=ON  SIRRENBERG CHRISTIAN/AU
L106          2 SEA ABB=ON  PLU=ON  ZENKE FRANK/AU
L107          3 SEA ABB=ON  PLU=ON  ((L100 OR L101 OR L102 OR L103 OR L104 OR
                L105 OR L106)) AND TYROSINE KINASE?
L108          0 SEA ABB=ON  PLU=ON  ((L100 OR L101 OR L102 OR L103 OR L104 OR
                L105 OR L106)) AND L64

     FILE 'STNGUIDE' ENTERED AT 13:52:17 ON 16 JUL 2008
                D COST
                D QUE L78
                D QUE L107

     FILE 'HCAPLUS, MEDLINE, EMBASE' ENTERED AT 13:53:35 ON 16 JUL 2008
L109          8 DUP REM L78 L107 (0 DUPLICATES REMOVED)
                      ANSWERS '1-5' FROM FILE HCAPLUS
                      ANSWERS '6-7' FROM FILE MEDLINE
                      ANSWER '8' FROM FILE EMBASE
                D L109 1-5 IBIB ABS
                D L109 6-8 IBIB AB
                D QUE L54
                D QUE L86
                D QUE L98

     FILE 'HCAPLUS, BIOSIS, EMBASE' ENTERED AT 13:54:57 ON 16 JUL 2008
L110         84 DUP REM L54 L86 L98 (0 DUPLICATES REMOVED)
                      ANSWERS '1-64' FROM FILE HCAPLUS
                      ANSWERS '65-72' FROM FILE BIOSIS
                      ANSWERS '73-84' FROM FILE EMBASE
                D L110 1-64 IBIB ABS FHITSTR HITIND
                D L110 65-84 IBIB AB HITIND
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